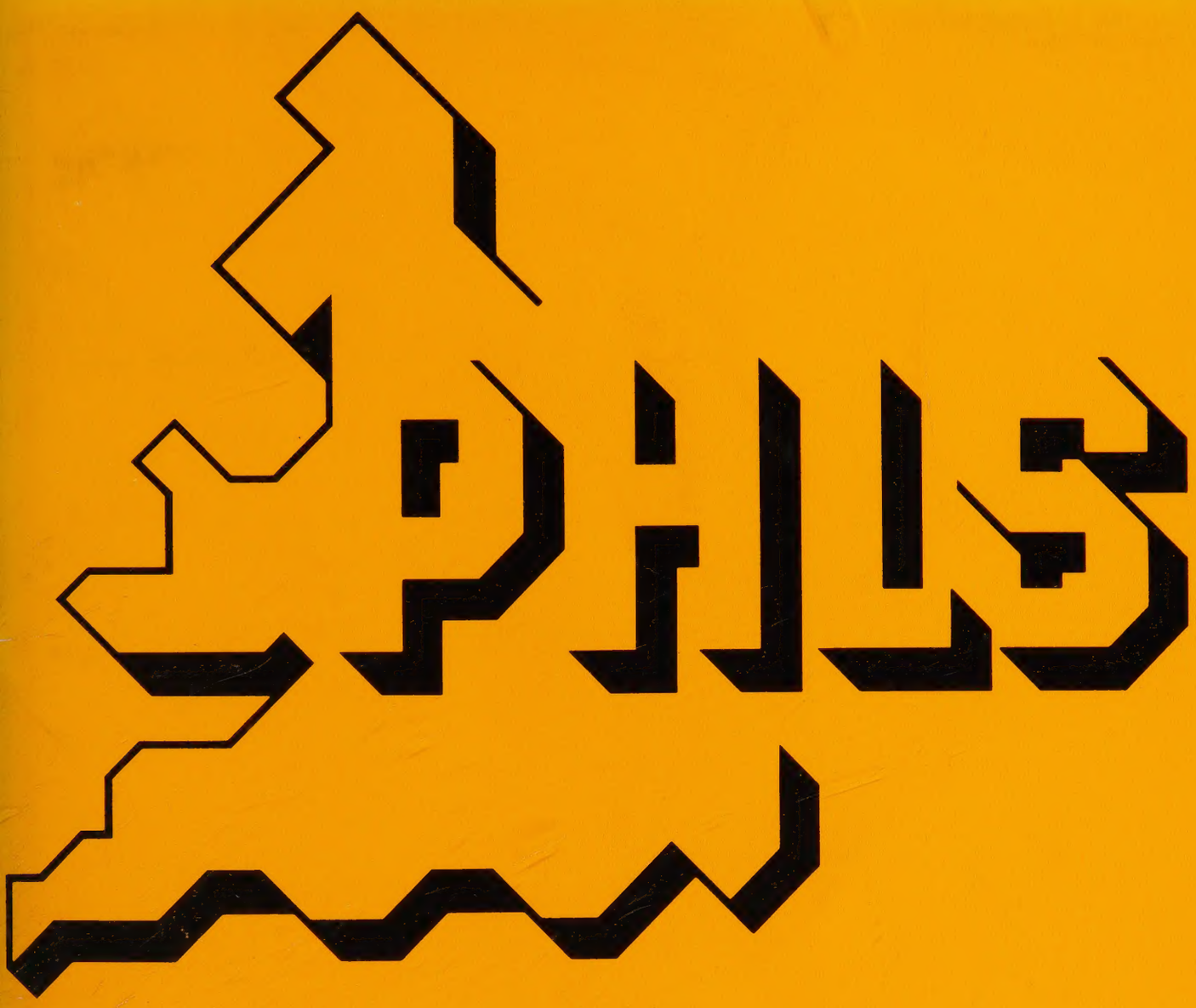

Public Health Laboratory Service
Annual Report 1980~1981

PUBLIC HEALTH LABORATORY SERVICE ANNUAL REPORT FOR 1980/81

ISSN 0142 3517
ISBN 0 091144 09 6

Published by the **Public Health Laboratory Service Board**
61 Colindale Avenue London NW9 5EQ

Printed by **Hobbs the Printers** Southampton SO9 2UZ (2233)

CONTENTS

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Chairman: **Professor M H Richmond**

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Chairman and Secretary to be appointed

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Chairman: **Dr J E M Whitehead**
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Dr D J H Payne
Dr B Rowe

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Working Party on Campylobacter Infections
Chairman: **Dr M B Skirrow**

REPORT ON THE WORK OF THE SERVICE
1980/81

Figure 1: Sir Robert Williams starting excavations for the foundations of the new Colindale.

Introduction

THE activities of the laboratories and other components of the Public Health Laboratory Service have become so many and various that it has become increasingly difficult to present a reasonably comprehensive account of them within the existing dimensions of the Annual Report. By varying the extent of the coverage given in different sections from year to year, it should be possible to ensure that the Report continues to encompass the activities of the whole Service, while providing more detailed information about particular parts of it, although at slightly longer intervals than before. For the Report for 1979/80, the 52 regional and area laboratories were invited to contribute short individual reports on their research and development activities; in this year's Report this aspect of their work has been summarised as a table (Table 3) and instead more space devoted to an account of the PHLS Centre for Applied Microbiology and Research (CAMR) during the second year of its existence, as its scientific work gathered momentum. Last year, reports from certain committees and working parties were included; this year these have been replaced by short accounts of five topics of current interest, some of which are in the purview of one or more of the committees or working parties of the PHLS.

Staff numbers

THE number of staff working in PHLS Laboratories at the end of March 1981 is shown in Table 1 and is little changed when compared with last year.

Table 1 Numbers of staff working in PHLS Laboratories at 31 March 1981

Grade	*Regional and Area Laboratories*			*Reference and Special*	
	PHLSB	RHA/AHA	Total	CPHL	CAMR
Consultants	90	21	111	15	3
Other Medical	49	25	74	9	1
Top Grade and Principal microbiologists	10	–	10	16	25
Other microbiologists	37	5	42	48	52
Technical Officers, Principal and Senior Chief MLSOs	48	23	71	12	5
Other MLSOs	734**	405**	1 139	60	68
Administrative and clerical	252	70	322	83	32
Maintenance and other	279	84	363	116	73
Totals	*1 499*	*633*	*2 132*	*359*	*259*

* Including 12 Computer Services Unit

** 30 MLSO staff transferred to PHLSB from Leicester AHA(T)

Laboratories

THE total number of regional and area laboratories is unchanged at 52. The laboratory at Conwy which had been established in converted accommodation in Bryn Hyfryd, a Victorian house with a fine view of Conwy Bay, since September 3rd, 1939, closed in May 1980 and was transferred to the new Vale of Clwyd district general hospital, Bodelwyddan, near Rhyl, where it forms a joint PHLS/hospital microbiology laboratory occupying some 850 square metres. Ownership of Bryn Hyfryd has reverted to the Welsh Office.

At Leicester, the PHLS laboratory at Groby Road Hospital transferred in November 1980 to new accommodation in the Clinical Sciences Building at the Leicester Royal Infirmary where it, too, forms a joint microbiology laboratory with the Leicester AHA (T) and occupies some 1300 square metres. The Board's contribution to the cost was approximately £210,000.

Plans for the new laboratory at Gloucester were completed during the year and those of the new laboratory at Ashford (to replace the Maidstone laboratory) reached an advanced stage.

The enabling works on the site of the new building for the Central Public Health Laboratory, Colindale were completed in September 1980 and in March 1981 authority was finally received from the Department of Health and Social Security to let the contract for construction of the main buildings in the sum of £15,291,000 (at May, 1980 prices).

Plans for a new Production Centre at the PHLS Centre for Applied Microbiology and Research (CAMR), Porton Down, for the preparation and purification of vaccines and other therapeutic substances were completed and submitted for the approval of the Department of Health and Social Security. Outline plans for a new Fermentation Pilot Plant have also been drawn up and submitted.

Laboratories			*Total in laboratories*		*Staff totals:*		
Others	RHA/ AHA	Total		HQ Office	*PHLSB*	*RHA/AHA*	*All*
7	–	25	136	2	117	21	138
2	–	12	86	–	61	25	86
6	–	47	57	1	58	–	58
15	–	115	157	–	152	5	157
3	1	21	92	–	68	24	92
23	5	156	1 295	–	885	410	1 295
29	1	145	467	52*	448	71	519
8	–	197	560	2	478	84	562
93	*7*	*718*	*2 850*	*57*	*2 267*	*640*	*2 907*

CENTRAL PUBLIC HEALTH LABORATORY

Acting Director (to 30 September 1980): Dr B Rowe
Director (from 1 October 1980): Professor A A Glynn

THE reference and research activities continue to grow, though restricted by serious overcrowding of the ageing buildings and huts in which they are carried on.

With the allocation at last of £15 million for the New Colindale Project, the year started well. When the lowest tenders proved slightly above the limit, a tense period of readjustment was needed to bring the costs down without losing anything vital. The eventual permission to proceed to contract arrived early in March 1981, shortly followed by the appearance of mechanical excavators on site, and to his own and everyone's delight, the Director of the Service, Sir Robert Williams, drove one to cut the first sod on April 10th.

Bacterial Metabolism Research Laboratory

(Dr M J Hill)

WORK continues on the relationship between gut bacteria, bile acids and cancer of the colon and between bacteria, nitrates and stomach cancer.

The effects of cimetidine, ranitidine and ascorbate on the flora and composition of gastric juices are being examined.

The use of gas-liquid chromatography and mass spectrometry in the identification of *Legionella pneumophila* is being explored, together with the use of enzyme profiles in the rapid identification of anaerobic bacteria.

The Laboratory will move to CAMR in December 1981.

Division of Enteric Pathogens

(Dr B Rowe)

THE division has now settled into its new quarters in the 1906 building. During the year the computer system for dealing with salmonella specimens and reports was finally commissioned. It is working well and should improve the efficiency of current surveillance and future analysis.

Serological and phage typing of *Salmonellae, Shigellae* and *E. coli* continue to expand and more new types have been found. Phage typing is often simpler and more economical than serotyping. A routine phage typing system for *Salmonella hadar* was introduced.

Meningitic strains of *E. coli* frequently carry the K1 antigen. This is a poor antigen and a phage recognition technique has been developed. A serotyping scheme has been developed for *Citrobacter koseri.* Serotyping of *Campylobacter* is relatively unsatisfactory and a phage typing scheme is being developed.

Much effort is being devoted to the study of the toxigenic, adhesive and invasive properties of *E. coli* strains causing diarrhoea. This is combined with examination of the genetic control of enterotoxins and adhesive factors.

Division of Hospital Infection

(*Dr P D Meers*)

THERE have been several recent outbreaks, some quite large, of skin sepsis due to group A streptococci. Though skin trauma is an essential initiating factor, typing sera developed at Colindale have allowed the recognition of characteristic strains which are not those normally found in throat swabs or causing pharyngitis.

Prospective surveys for infection with group B streptococci have been completed and collaboration with St Mary's Hospital continues. The phage typing method developed in the laboratory has proved useful and is being adopted by others.

Surveys of gentamicin and methicillin resistance in *Staphylococcus aureus* have been completed. Screening for plasmid DNA has been added to the typing methods used for investigating outbreaks of staphyloccal infection, but the methods need developing further.

The study on the taxonomy of *Staphylococcus albus* is nearing completion.

Development of the serological typing of *Pseudomonas aeruginosa* continues and a typing scheme for *Enterobacter* is being developed.

Numerous investigations in collaboration with clinicians include studies of infection in orthopaedic operations and in children with cystic fibrosis.

A project on the microbiology of hospital hot water systems, listed as minor, provided timely information of help in dealing with the legionella outbreaks.

A major effort was the completion of the National Survey of infection in hospitals, which involved 18 163 patients in 43 hospitals. Analysis of the results is in progress. An associated activity was to contribute to the further education of infection control nurses.

Division of Microbiological Reagents and Quality Control

(*Dr P S Gardner*)

THE number of laboratories participating in the National and International Quality Control Schemes continues to increase. There has been a great increase in the number of virus distributions and a pilot scheme for antibiotic sensitivity testing has been introduced. More freeze dried specimens are being sent out.

Work continues on legionella antigens and reagents are issued to PHLS reference laboratories and some laboratories abroad. Counter-current, microagglutination and ELISA techniques are being evaluated for the diagnosis of legionnaires' disease.

A phage typing system for *Listeria monocytogenes* is being developed in collaboration with the University of Tours, France.

New immunofluorescent reagents have been issued for the rapid diagnosis of influenza A, influenza B, RSV, parainfluenza 3, measles, herpes and rotavirus infections. Rationalisation of viral and bacterial reagents continues.

Work is also going on to improve the diagnosis of hepatitis and rubella. Some monoclonal antibodies to adenovirus 5 have been made.

Epidemiological Research Laboratory

(*Dr T M Pollock*)

THE main effort of the laboratory continues to be directed to whooping cough vaccine. Its efficacy is being assessed by a study made with 21 Area Health Authorities in England, of whooping cough notifications in vaccinated and unvaccinated children. Social conditions and other relevant factors are taken into account. The field work has been completed and the results are now being analysed.

Three studies are in progress on reactions to diphtheria, tetanus and pertussis vaccine. The field work of the very detailed survey in Hertfordshire is now finished and the results are being analysed. Reactions to the vaccine in the North West Thames Region are still being recorded. The relationship of laboratory toxicity tests to reactions in infants is being examined in conjunction with the National Institute for Biological Standards and Control.

Studies of viral hepatitis in diagnostic units and travellers continue in association with the Virus Reference Laboratory and the Communicable Disease Surveillance Centre. Antibodies to A and B virus are being measured and sera stored for subsequent study when candidate viruses for non-A, non-B hepatitis are investigated. The protective value of immunoglobulin and its minimal effective dose are being assessed.

Other studies include the surveillance of rubella and measles vaccination results and the long term effects of virus infections in infancy.

Food Hygiene Laboratory

(*Dr R J Gilbert*)

IN addition to its normal bacteriological examination of foods, the laboratory this year has been involved in some more exotic investigations. Methods have been developed for detecting paralytic shellfish poison and ciguatera toxin (with MAFF Fisheries Laboratory, Burnham on Crouch) and for haemagglutinins in red kidney beans (with Queen Elizabeth College, London). Scombrotoxic fish poisoning has also been investigated (with MAFF Torry Research Station, Aberdeen).

Clostridium perfringens still provides much work. Carriage by normal populations varies, but a survey (with PHLS Lincoln) shows that long stay geriatric patients may excrete very large numbers of this organism. About 80% of strains from food poisoning outbreaks are toxigenic; the figures are much lower for strains from other sources.

Serological typing has been used to investigate cross-contamination in poultry processing plants (with Food Research Institute, Norwich).

Other studies include the application of ELISA to *Staphylococcus* aureus enterotoxin, and of radio-immune assay to *Bacillus cereus* toxin.

Leptospira Reference Laboratory

(*Dr Joyce Coghlan*)

IN the development of improved methods for the diagnosis of leptospira infection, ultracentrifugation has proved helpful in the preparation of specific antigen fractions. Detection of antibodies by ELISA is being investigated, but there are still problems. The laboratory is collaborating with the Sub-Committee on the Taxonomy of Leptospira by typing difficult strains with a view to improving the serological classification.

A new British serotype of the Tarassovi serogroup has been identified and confirmed by others. A strain of the cattle serotype *hardju* was isolated from man for the first time.

National Collection of Type Cultures

(Dr L R Hill)

AS a background to its provision of authenticated cultures and to its diagnostic services for difficult or unusual organisms, the NCTC carries out taxonomic studies based on phenotypic data combined with DNA base composition determinations. The aim is to revise the classification and improve the identification of clinical isolates.

Many of the organisms sent for identification are species of *Pseudomonas or Corynebacteria.* In the former a comparison of DNA data with the results of whole cell protein electrophoresis is being made in collaboration with the Hospital for Diseases of the Skin.

New techniques for examining DNA—DNA hybridisation in vitro include the nick translation method of in-vitro labelling. This will be particularly useful with organisms such as *Campylobacter* and coryneforms, whose DNA is difficult to label in vivo. The cell fatty acid composition of *Campylobacter* is being examined by gas liquid chromatrography.

The computer identification summaries for gram-negative fermenters and non-fermenters have been completed.

Legionella and Legionella-like organisms form a significant portion of the new strains added to the collection. The demands on freeze-drying capacity increase steadily.

Virus Reference Laboratory

(Dr M S Pereira)

THE use of virus isolation and identification methods in tissue culture is being superseded by rapid immunofluorescent techniques and new sensitive methods of detecting antibodies. For agents not yet cultivable direct electron microscopy of specimens is becoming more fruitful.

New or improved radio immunoassays are being developed for rabies, hepatitis, herpes zoster and Coxsackie B antibodies. Antibody capture techniques for measuring IgM antibodies are proving successful.

The study of polyoma viruses in pregnancy and in transplant patients continues and now includes restriction enzyme analysis of viral DNA for distinguishing new strains. The study continues of the unclassified parvovirus-like agents discovered by electron microscopy in the faeces from some outbreaks of gastroenteritis.

Antibodies to Epstein-Barr virus are being studied in patients with rheumatoid arthritis or receiving transplants (in conjunction with University College Hospital and PHLS Bath).

A start has been made on the development of monoclonal antibodies to influenza virus antigens.

CENTRE FOR APPLIED MICROBIOLOGY AND RESEARCH

Director: Dr P M Sutton

1980/81 is the second year of CAMR's existence as part of the PHLS, but is the first in which the scientific programme has become fully operational, for the Centre is now completely staffed and most of the laboratories are occupying their definitive sites in the building.

The reports of the directors of the nine constituent laboratories on their scientific work are summarised below together with the report of the Deputy Director on income generation, an activity of considerable importance at CAMR. Some other features of the year's events are first singled out for special mention.

Laboratory changes

Following Dr K Sargeant's resignation as Director of the Microbial Products Development and Production Laboratory a new laboratory was created by fusing the Microbial Products Development and Production Laboratory with the Diagnostic Reagents Laboratory. It has been named the Microbial Technology Laboratory, to be directed by Dr A Atkinson.

As this year will see the transfer of the Bacterial Metabolism Research Laboratory from Colindale to Porton, two areas, of some 300 square metres, are being converted for the biochemical and microbiological sections of BMRL. The move of this laboratory will further strengthen the Centre's scientific programme, as well as bringing an increase to the analytical biochemistry facilities at CAMR.

Long term capital developments

Formal approval for the CAMR Development Plan (Production Centre and Fermentation Pilot Plant) has now been given by DHSS. Approval for the detailed design of the Production Centre is expected in Autumn 1981; any prolonged delay will have serious consequences for the scientific programme, especially in the field of vaccine production.

Biotechnology

CAMR has an important role to play in the development of biotechnology in the United Kingdom and this is acknowledged by the Centre being singled out for special mention in the White Paper on Biotechnology (Cmnd 8177) which was published in March 1981. It is clear that the general approach of CAMR to biotechnology is in line with governmental policy.

Outside contacts and academic programme

Many contacts exist and more are being fostered between CAMR and the rest of PHLS, as well as with universities and other research institutes; three of the laboratory directors are Visiting Professors.

The academic programme for the Centre comprises weekly internal lectures and a series of monthly lectures from outside visitors, the highlight of the year being the David Henderson Memorial Lecture, delivered by Professor J R Postgate, FRS.

Engineering

This year a report is included on the work of the Engineering Group whose activities are a key element in many of the scientific projects undertaken by the Centre.

Income Generating Activities

Mr R Holmes

Research grants from public bodies

Four research grants, with a total annual value of £72 000, were received; two from the Medical Research Council, one from the Wessex Area Health Authority and one from the Department of Environment. When continuing grants from the Cancer Research Campaign and Health and Safety Executive are added, the total annual grant support amounts to approximately £150 000. These funds are used largely to offset the costs of additional short-term staff needed to supplement existing resources for a range of projects.

Research agreements with commercial firms

Three additional agreements were made with commercial firms, viz: Technoferm Developments Limited, Unilever, and Instrumentation Laboratories Inc.; when the existing funding from Cadbury Schweppes is added, the annual value of this type of income totals £112 000.

Other commercial contracts

A new agreement of major importance to CAMR is that with KabiVitrum Limited. This provides for CAMR to scale-up and develop a process to manufacture human growth hormone by the use of genetically engineered bacteria. The agreement also allows for future UK requirements of the hormone to be produced at CAMR by this means, thus eventually replacing the present process at CAMR of extracting human growth hormone from pituitary glands.

Contracts have been signed with three firms which will result in on-going royalty payments to PHLS for use of patents, products and processes developed at CAMR. This category of income should increase in future as additional patent applications are submitted and exploited by industry under licence agreements.

Sale of products

This is a major source of income. Demand for asparaginase in the treatment of leukaemia continues to increase and income in the past year will exceed £300 000. The sale of microbial products, mainly bacterial cell pastes, has realised approximately £80 000. In future greater emphasis will be given towards establishing firm long-term contracts with major users of particular products. However, with continuing support from the MRC and SRC, it is intended to continue the supply of microbial products for academic research, although not all may be available off the shelf.

Activities providing savings for the Health Services

Although not strictly income-generating, substantial CAMR resources are devoted to producing materials required for health care which are not available in the UK market, or if available, are not satisfactory. These include the extraction of human growth hormone, the manufacture of anthrax vaccine, botulinum toxoids, Kveim test antigen for sarcoidosis, and the provision of tissue culture cells for virology laboratories. These activities are either funded at cost by DHSS or carried out as part of the base programme of CAMR.

Future prospects

These are promising. In addition to the exploitation of new products and processes currently under development, discussions are in progress with several commercial firms

on projects of mutual interest. Consultations are also continuing with the National Research Development Corporation, the National Enterprise Board and with Celltech, on ways in which CAMR can contribute, within its resources and remit, to the further development of biotechnology in the UK.

A summary of income (provisional for the financial year 1980/81) is given in Table 2.

Table 2 Provisional Income CAMR*

	£ 000
Research and development projects	
Public bodies	135
Industry	98
Receipts from sale of products	
to DHSS and NHS	432
to others	417
Royalties etc	10
Payment for services and facilities	74
Sub total	1 166
DHSS Chief Scientist's Office (research programmes)	717
Total	£1 883

* Figures given are for cash received and may be less than full year value for new contracts.

Special Pathogens Reference Laboratory

Professor D I H Simpson

SOME 900 specimens were received from this country and from abroad for serological tests for arbovirus infections; several cases of dengue fever, West Nile encephalitis and chikungunya were diagnosed.

Five isolations of Lassa virus were made, one from an acutely ill patient in Nigeria, and four from the blood of small mammals (*Mastomys natalensis*) sent from Sierra Leone. Specimens from 42 patients in the UK were examined to exclude viral haemorrhagic fever.

A diagnostic service for rickettsial infections was also begun, using both indirect haemmagglutination and fluorescence techniques.

Lassa and Mozambique viruses

Research has continued into the differences between these two viruses. Their growth kinetics in tissue culture differ, the Mozambique virus growing more rapidly than Lassa. The ultrastructure of the Mozambique virus is consistent with the development and morphology of an arenavirus but does not show the pleomorphism of Lassa virus. The close relationship between these two viruses is, however, apparent from the results of

plaque reduction tests in tissue cultures, which accord with those obtained by immunofluorescence and complement fixation tests. The antigenic relationships between these two viruses are being further investigated using monoclonal antibodies against lymphocytic choriomeningitis virus. Attempts are also being made to produce monoclonal antibodies against Lassa and Mozambique viruses themselves.

Ebola virus

Experimental infections in monkeys have been treated with convalescent plasma at different intervals after infection, with some delay in the onset of viraemia, but with little effect on survival. Further studies are planned using a combination of convalescent plasma, interferon and ribavirin.

Pathogenic Microbes Research Laboratory

Professor D C Ellwood

THE primary research interests of this laboratory centre around *Bordetella pertussis*, animal models of infectious disease and oral microbiology.

Bordetella pertussis

In research aimed at developing an improved whooping cough vaccine, two protective antigens—originally designated fimbrial haemagglutinin (FHG) and outer membrane protein (OMP)—have been identified. Evidence for their being separate and distinct components rests on the observations that both antigens have only minor chemical features in common and that, whereas FHG is present only in static cultures, OMP is expressed in both static and shaken cultures. However, Tris-NaCl extracts from static cultures do contain both antigens. Cross absorption experiments with homologous and heterologous antisera have proved inconclusive so far.

FHG shows mouse protective activity and low toxicity. The major component probably has a molecular weight of 220 000. The low yield of this antigen in culture has been tackled by altering the growth conditions, and some success has resulted in defining the medium to give FHG-producing colonies. A sandwich-type ELISA technique has been developed to measure FHG, and hence monitor production of the antigen under varying experimental conditions.

OMP also looks promising, as it is highly antigenic and relatively non-toxic to mice, provided the lipopolysaccharide is first removed by detergent-column chromatography. Further purification of the antigen by column chromatography is under way, and one protein of molecular weight 74 000 is known to be present. ELISA assays are used to examine sera and respiratory tract washings of rabbits immunised with preparations of these antigens and later challenged by intranasal instillation of *B. pertussis*. Sera from children whose history of whooping cough and pertussis immunisation is known will be assayed for antibodies to FHG and OMP. Finally, a monoclonal antibody to FHG has been derived and will be used to analyse the structure of this antigen, as well as being employed in assay systems.

The mouse protective efficacy of these OMP and FHG preparations is being independently assessed at the National Institute of Biological Standards and Control.

Animal models of infectious disease

Campylobacter infection Oral infection of Rhesus monkeys with *C. jejuni* has proved a suitable experimental system. The animals developed bacteraemia after 1–3 days, and

although they were resistant to reinfection after recovery, it was not usually possible to detect circulating antibodies.

Legionella pneumophila In the search for a suitable experimental host, a wide variety of animal species have been challenged with the organism, but to date only guinea-pigs have proved to be susceptible—by intraperitoneal injection. Small particle aerosols containing the microbe are being investigated as a means of initiating infection. Support has been given to the Environmental Hygiene Reference Laboratory in examining water samples for legionella by guinea-pig inoculation.

Other studies Collaboration with the PHLS laboratory at the Central Middlesex Hospital, on human calicivirus, and with the Vaccine Research and Production Laboratory at CAMR, on tick-borne encephalitis virus is continuing.

Oral microbiology

Dental caries Acid production by the oral bacteria from dietary carbohydrate is a major factor in the pathogenesis of caries. Studies have been made of the metabolic pathways involved, and how these are affected by cation concentration, and have led to the suggestion of alternative biochemical mechanisms, whereby streptococci take up sugars.

Chemostat models of oral microbial populations Much controversy surrounds the question of the bacterial specificity of dental disease, and whether or not this is a problem of mixed populations of microbes. Chemostat models of dental plaque are being examined to see how a commensal population of bacteria can become pathogenic, and cause dental disease.

Services to other CAMR laboratories

These are substantial and include gas chromatography, electron microscopy, animal wing, media preparation and autoclaving, and wash-up.

Vaccine Research and Production Laboratory

Professor J Melling

Production

Anthrax vaccine Two final batches were produced at the licensed unit at Allington Farm, Porton, before the building was handed back to the Ministry of Defence in April, 1980.

Vaccinia Potency testing of the national reserve stock has shown no significant loss of titre of the freeze-dried smallpox vaccine. Two extra trial batches of vaccinia have been produced by the traditional Lister method, using sheep.

Kveim antigen This skin test reagent for the diagnosis of sarcoidosis was also produced at CAMR, in conjunction with the PHLS Central Public Health Laboratory, Colindale, and the Brompton Hospital.

Tissue cells 6000 cultures of monkey kidney cells and 2000 cultures of human diploid cells (MRC−5) were sent out from CAMR this year to 43 PHLS and 30 other laboratories. The kidney cell cultures are now prepared by a more efficient and less expensive method, and the cells are dispatched from Porton in gelatin suspensions—rather than in monolayers in roller bottles as previously—with consequent further economies.

Avian myeloblastosis virus (AVM) 150 litres of high titre AVM plasma, from which reverse transcriptase will be purified, was produced to meet requests from America and Germany.

Herpes simplex virus (HSV) vaccine In conjunction with Birmingham University, 8 batches of an acetone-extracted sub-unit vaccine, derived from type I HSV, were produced. These are undergoing tests in animals with promising results.

Research

Cytomegalovirus (CMV) The development of a sub-unit vaccine against human CMV infection, which can cause birth defects, and complications in patients receiving organ transplants, is a major aim of the laboratory. The Ad 169 vaccine strain was grown on MRC−5 cells, harvested and purified. A laboratory animal model is being sought, so far without success.

Herpes simplex virus vaccine. This work falls into two parts; the development of a tissue culture system capable of producing high yields of HSV, and the further treatment of the whole virus particle to yield a sub-unit vaccine.

Two tissue culture approaches have been tried: a microcarrier system of spherical carriers in suspension and the glass bead column. So far, the amount of virus produced has not kept pace with the increased cell yield.

Virus specific antigen has been prepared by harvesting the vesicles of plasma membrane released from infected cells into the surrounding medium, and has been found to protect guinea-pigs from lethal infection after challenge by the genital route with HSV type 2. Both humoral and cell-mediated immune responses are being measured to gauge the efficacy of these experimental vaccines.

Monoclonal antibodies This technology is potentially of great importance both for monitoring the antigenic composition of pathogens and their attenuated derivates and for development as therapeutic substances. An initial project with the Pathogenic Microbes Research Laboratory (see p.25) was successful in producing a monoclonal antibody against the fimbrial haemagglutinin of *B. pertussis.* The technique is now being used to compare the antigenicity of wild tickborne encephalitis virus (TBEV) with the killed vaccine prepared from it.

Plasmid stability Knowledge of the factors affecting the stability of antibiotic resistant plasmids in bacterial hosts is of fundamental importance where genetically manipulated microorganisms are used as sources of biologically active products. A series of plasmids, all suitable for cloning foreign DNA into bacterial hosts, has been studied in *E. coli* and *B. subtilis* under varying conditions of continuous culture.

Tick-borne encephalitis vaccine assessment The pathological effects of TBEV on unprotected animals (monkeys and sheep) and the protection afforded by vaccination have been studied extensively. Data have been collected on the many clinical biochemical, histological and virological accompaniments of the infection as well as on the immune response to the vaccine. In the course of the study two major viral surface antigens were identified.

Clostridium botulinum toxins and toxoids This organism is grown in enclosed fermenters ('pomecs') and regular batches of toxins types A, B, E and F produced: work on toxins types C and D, in stirred fermenters, will begin soon. In addition *Cl. botulinum* type A is being grown in continuous culture.

A standardised procedure for extracting and purifying type A haemagglutinin-neurotoxin complex for use in preparing toxoid has been established. Work is proceeding on the other toxin types.

The first production run of type A toxoid, for human clinical use, is under way.

Other studies Collaborative work is in progress on possible biochemical markers of poliomyelitis vaccine, on *Cl. difficile* toxin, on biochemical changes in experimental

legionella infection, as well as research on the possibility of producing a 'therapeutic' vaccine against penicillin-resistant ß-lactamase-producing gonococci.

Microbial Products Development and Production Laboratory

Dr K Sargeant (until 24.12.80)
Mr C G T Evans (Acting Director from 25.12.80 to 31.3.81)

MOST of the effort at the Fermentation Pilot Plant (FPP) has been devoted to production activities, or to preparing for new types of production, notably for growth hormone. The main products have been enzymes for other CAMR laboratories including asparaginase, glutaminase and phenylalanine ammonia lyase (PAL) and carboxypeptidase, as well as smaller amounts of other research materials.

Human growth hormone (hGH)

A contract has been signed with KabiVitrum AB (the State-owned Swedish pharmaceutical company), whereby CAMR will collaborate in the fermentation scale-up (i.e. from 10 litres to 400 litres) of the hGH synthesising, genetically manipulated strain of *E. coli*, previously developed for Kabi by the American company, Genentech. The aim is to develop a routine production process for the manufacture of the hormone for clinical use in the treatment of pituitary dwarfism.

Permission had first to be obtained from the Genetic Manipulation Advisory Group and this was granted after a site inspection but was conditional upon the organisms being killed in the fermentation vessel at the end of the process. How to kill the bacteria without damaging the hormone presents a considerable technical problem. There is little doubt that within a few years all the hGH needed clinically will be produced microbiologically, and the need to salvage this hormone from autopsied human pituitaries will vanish.

Asparaginase

The Medicines Inspectorate visited the FPP, following application by PHLS for CAMR to be granted a Manufacturing Licence to produce asparaginase. Their subsequent report made certain recommendations about improvements at the FPP, which are being acted upon.

Toxic substances in the environment

Under a research contract with the Department of the Environment, a study has begun on the use of microbes to degrade certain aromatic chlorhydrocarbons, and on the sequestration of heavy metals in the environment.

External sales

For many years the FPP has produced a wide variety of microbial products—including bacterial cell pastes, bacteriophages and enzymes—for outside organisations. The existing catalogue of these products has been reviewed and a streamlined, more limited range will be available in future. One of the items likely to be retained are spores of *Bacillus globigii*, used by Water Authorities as tracers.

Outside research groups

Both Cadbury Schweppes and Technoferm have rented space at the FPP for research into biotechnology.

The new Fermentation Pilot Plant

A PHLS Scientific Review Committee visited the laboratory in December, 1980 and reported favourably on the past scientific achievements and present research interests of the laboratory. It strongly endorsed the need for a new FPP, on the main CAMR campus, and discussions are under way on the specifications, especially the size of the large fermenters, and the degree of containment needed for the future.

Therapeutic Products Laboratory

Dr H E Wade

Therapeutic enzymes

Asparaginase This enzyme continues to be needed in the combined therapy employed to maintain remission in acute lymphoblastic leukaemia in children. It has played an important part in the improved survival times now being found in this disease.

During the year, 294 megaunits of asparaginase were distributed: 116 to UK hospitals, 120 to the USA and 58 to other overseas hospitals.

Glutaminase The problem of producing glutaminase, from *Achromobacter*, free of contaminating proteases has not yet been solved. Currently the present methods of the initial extraction at the FPP are being modified in an attempt to solve this.

Phenylalanine ammonia lyase (PAL) The oral treatment of the inborn error of metabolism, phenylketonuria (PKU) is now regarded as the most promising use of this enzyme. The problems to be solved are to increase the yield of PAL from *Rhodotorula glutinis*, to improve its palatability, and to evaluate this treatment clinically.

The first has been tackled by seeking changes, both phenotypic (via alterations in the medium used) and genotypic (through strain selection). The approach to the second has been to attempt to prolong the life of PAL in the small bowel by using enteric coated capsules, and also by modifying PAL chemically to decrease its sensitivity to enzymatic breakdown by the digestive juices. However, the latter has been unsuccessful and attention is being directed to providing a physical barrier to enzymatic breakdown. Clinical trials will be conducted by the MRC Unit of Toxicology and Queen Mary's Hospital for Children, Carshalton. Two commercial firms have shown an interest in marketing PAL for oral treatment.

The possible anticancer effects of PAL have not been discounted and are to be further evaluated, using xenografts of human malignant melanoma.

Histidinase and methioninase Although adequate amounts of purified histidinase can now readily be produced, recent experimental work at CAMR on its effect on a wide variety of transplantable murine tumours has been discouraging. For methioninase, however, there is some recent evidence that it may be of value in the treatment of myeloid leukaemia.

Human growth hormone In 1979 the laboratory accepted two responsibilities on behalf of the DHSS: the central collection of autopsied human pituitaries and the extraction of human growth hormone (hGH). These were extended in 1980 to include the extraction of gonadotrophins as well.

Both frozen and acetone-fixed pituitary glands are stored at CAMR, and a system of documentation has been introduced to facilitate computer monitoring of the collection and the extraction process. The frozen glands are dispatched for commercial processing; acetone preserved pituitaries are treated at CAMR by a modification of the Stockell-Hartree method, originally developed at Cambridge. This Porton modification yields a

monomeric preparation, less allergic than that previously available. In addition, stocks of partially prepared pituitary powder, previously stored at Cambridge, have also been purified to yield hGH.

In spite of many problems experienced over the past year, over 250 000 units of hGH have been dispatched for freeze-drying and ampouling, ready for use. Recent improvements in the extraction techniques are expected to increase the yield of hormone.

The extraction levels of gonadotrophins from the pituitary glands have been satisfactory, and a substantial quantity has been supplied to other centres, for use in hormone assay kits.

Freeze drying The laboratory has carried out a wide variety of routine freeze-drying activities for other CAMR labs, and for the Central Public Health Laboratory, as well as for outside customers. Improvements have been made in the freeze-drying of rubella antisera and hGH, as well as other substances.

Analytical chemistry The section gives an important service to the rest of the Centre, over 10 000 separate analyses being performed during the year.

Diagnostic Reagents Laboratory

Dr A Atkinson

THE laboratory completed its moves into its definitive space in the main CAMR building. In spite of some inevitable disruption, the scientific programme has gone ahead.

Plasmid vectors for genetic manipulation

In all, 155 strains of thermophilic bacilli have been screened for antibiotic resistance, or bacteriocin production, and six have been found to contain plasmids which have been further characterised.

Alternative hosts in genetic manipulation

Research has continued into the use of bacilli and yeasts as hosts for a variety of plasmid vectors. A remarkable stability, with preservation of copy numbers, of a plasmid (and its derivative) originally isolated from an antibiotic resistant host, has been shown in *B. subtilis*, even in the absence of antibiotic selection pressure. This is being investigated.

Breakdown of paraquat

A soil yeast, capable of degrading the toxic herbicide paraquat (1,1′-dimethyl-4, 4′-dipyridylium dichloride) has been studied as well as the metabolic responses of a selection of microorganisms to the weedkiller. The difference among species to its toxicity was wide.

Carboxypeptidase G

The laboratory has been supplying Charing Cross Hospital with carboxypeptidase G for clinical evaluation, as it reduces the side effects of chemotherapy. Scale-up of production at CAMR has continued.

Recently the substance has been modified by glycosylation, giving greater enzymatic stability and hence longer plasma life, and also by linking it to tumour-specific antibodies to direct it to malignant tissue.

Paracetamol
A new enzymatic method for the determination of serum paracetamol has been developed successfully that is rapid, sensitive and simple. Two provisional patent specifications have been filed and practical exploitation of the system is proceeding actively.

Procion dye matrices
Reactive triazine dyes have been used to purify many proteins by affinity chromatography now that the problems created by the heterogeneity of structure of the commercially available dyes have been overcome. Recently, the two techniques of affinity chromatography and high performance liquid chromatography (HPLC) have been combined into a new chromatographic approach termed high performance liquid affinity chromatography (HPLAC). HPLAC combines biological specificity with the speed, resolution and sensitivity of conventional HPLC and is the subject of a preliminary patent specification. Triazine dye HPLAC should have a wide application in many areas of clinical biochemistry especially where there is need for the rapid separation of biologically important macromolecules.

Other diagnostic enzymes
Work on glycerokinase has almost ceased now that the patent has been licensed commercially. The development of glycerol dehydrogenase, for assaying triglycerides in the study of heart disease, continues, as does work on luciferase, which is an adjunct in the assay of a number of other enzymes. Both enzymes are of commerical interest.

Schizophrenia and other abnormal mental states
A peptide has been isolated in high concentrations from the sera of patients suffering from schizophrenia, and some other psychotic states, compared with normal controls. The peptide, which is being purified, appears to block opiate receptors in animals.

Microbiological diagnostic reagents
Research has continued on the development of ß-lactamases for use in antibiotic assays, and also on an active enzyme, Protein A conjugate, for use in an ELISA system.

Cadmium monitoring and removal from the environment
This study is part of the research contract with the Department of the Environment, aimed at removing this toxic metal from trade effluents that contain cadmium cyanide.

Genetic Manipulation Laboratory

Dr P J Greenaway

THE structure and function of animal viral genomes, and of specific prokaryotic genes, are the main research interests in which studies were carried out.

Bordetella pertussis
For two years attempts have been made to manipulate genetically the genes coding for specific antigens of *B. pertussis,* with an emphasis on gaining expression in *E. coli* of the fimbrial haemagglutinin. Banks of *B. pertussis* genes have been constructed and screened for expression of different antigens, so far without success. Insertion frequencies were poor and the DNA insert was of low average size. Alternative methods of insertion, in particular the so-called 'tailing' procedure, a cosmid cloning strategy, and fractionating the DNA fragments before cloning have overcome these difficulties.

Human cytomegalovirus (HCMV)

Further information is being sought on the molecular organisation of HCMV DNA, and on the molecular biology of HCMV infections. In order to clone the virus into *E. coli*, recombinant plasmids have been constructed, each containing a different fragment of the HCMV genome: specific regions of the viral genome have been characterised in detail by restriction endonuclease digestion.

Studies of the expression of viral antigen in *E. coli* have been made possible by the co-operation of other PHLS laboratories in providing high titre antisera against HCMV.

Further work on HCMV will be supported by an MRC research grant.

Human papovaviruses

Many papovaviruses are difficult to grow, and hence to characterise, so their molecular biology is less well understood than that of some other viruses. BK, AS and JC viruses can produce persistent, or latent, infections in man. Initial experiments, in collaboration with the PHLS Virus Reference Laboratory, Colindale, have resulted in the molecular cloning in *E. coli* of biologically active BK virus DNA.

Other studies

A collaborative research programme has started with the Armand Frappier Research Institute, Quebec, on DNA recombination enzymes.

Microbiological Safety Reference Laboratory

Dr A E Wright

Research and development

AT the request of the DHSS, seven items of laboratory apparatus, mostly centrifuges and other equipment used for spinning, have been tested for the generation of potentially hazardous aerosols. The results have been communicated as confidential reports to the DHSS; it is hoped that, in the future, these will be published in the appropriate journals.

The development and testing of safety cabinets remains a high priority. Class 1 cabinets in use in routine diagnostic work were tested in 10 PHLS laboratories in a survey supported by a grant from DHSS. The high containment suites in use or being commissioned at Colindale, Leeds and Birmingham, as well as the Virus Laboratory at Ruchill, Glasgow, have been visited and their Class 3 cabinets and other equipment tested.

A study of the glues used to join plastic tubing in laboratories and hospitals (e.g. in dialysis systems) has shown that, far from supporting microbial growth—as had been suspected—the glues tended to be growth inhibiting.

Other researches included an investigation of the aerosol stability of *E. coli* strains used in genetic manipulation, and collaboration with the PHLS Communicable Diseases Surveillance Centre into the possibility of airborne spread of *Legionella pneumophila* in outbreaks at hospitals in Kingston and Cardiff.

Safety training

All new laboratory staff at CAMR undergo a course of training in safety in this laboratory. A videotape on safety has been prepared with DHSS, and the laboratory's 'standard display' on safety matters has been mounted at least 12 times, both inside and outside CAMR.

Safety services for CAMR

The Centre has over 70 Class 3 cabinets and these are tested at six-monthly intervals. The three existing high containment suites at CAMR are tested at six-monthly intervals, and inspected every three months. Over 60 rooms were fumigated during the year, either as routine maintenance, or because of changed microbiological use. The sewage from the effluent treatment plants at CAMR is tested before discharge outside the building. Finally, the quality control of some microbial products, the freeze-drying of pathogens, the identification of agents and the ordering and recording of freeze-dried stock cultures, are all part of the laboratory's routine activities.

Staff medical matters

These include scrutiny of the routine medical questionnaires completed by all new staff, the immunisation programme, which is now on a computer recall system and the surveillance of all accidents at CAMR.

Outside activities

Members of the staff have been consulted by the new David Bruce Vaccine Laboratory and Gatwick Airport, amongst many others, on problems in microbiological safety. Close links exist with WHO, and the laboratory is now designated as a WHO Collaborating Laboratory.

Environmental Hygiene Reference Laboratory

Dr G I Barrow

THE work of the laboratory concentrates upon problems of water contamination by microorganisms. To this end a study has started on the distribution of pathogenic free-living amoebae in the environment, and the role of these organisms in purulent non-bacterial meningo-encephalitis. Work on the identification and serological typing of strains of *Vibrio parahaemolyticus*, mostly from abroad, has continued.

In collaboration with the FPP and a Water Authority, field work has been carried out on the use of organisms produced at CAMR as microbial tracers to assess the dispersal of sewage at sea, with a view to advising on the best location for a new outfall.

Finally, the laboratory has also assisted other PHLS laboratories in screening water systems for *Legionella pneumophila*.

Engineering Department

Mr J F H Peel

BOTH the design and production facilities of the department have been stretched to their fullest extent and outside assistance had to be called in for both design work, and for part of the production programme, particularly where multiple quantities were required. Well over 1100 separate requisitions were received and a comparable number completed. Where outside contractors were used, specifications and drawings prepared by the engineering staff were issued and quality control maintained through our CAMR engineering staff.

Most of the work has been for laboratories within the Centre and the main priority was given to fitting out the Therapeutic Products Laboratory for the extraction of hGH for which special purpose safety cabinets and centrifuge housings were designed and

constructed. Sets of fermentation equipment have been assembled for the Microbial Products Laboratory, much of it in stainless steel. Prototype special purpose cabinets have been built for the Special Pathogens Laboratory whose high containment facilities are also serviced, with renewal of components as needed. Installation and commissioning of autoclaves in high containment laboratories in the Animal Wing has been carried out as has also the design and production of specialised items of equipment for various other laboratories at CAMR.

Assistance has been given to other PHLS laboratories with the installation and testing of the equipment produced for the high containment laboratories at Leeds, Birmingham and Liverpool, and similarly also the Glasgow Area Health Authority's laboratory at Ruchill Hospital. Special equipment items of Porton design has been made for Zurich University and Immuno Ltd.

COMMUNICABLE DISEASE SURVEILLANCE CENTRE

Director: Dr N S Galbraith

THE purpose-built accommodation for CDSC which was completed in January 1980 was formally opened by Sir Henry Yellowlees, the Chief Medical Officer of the DHSS, on 11th July; Dr Gordon Smith, Chairman, PHLS Board welcomed Sir Henry, and members of the Board and senior PHLS staff were shown the building and the work of the Centre.

During the year there were altogether 268 visitors, 113 of them from overseas; considerable interest was shown in the design and function of the Centre by European countries, particularly because it is the first purpose built surveillance centre in Europe. Informal links with several of these countries were developed; senior members of staff visited the Instituto Superiore di Sanità in Rome, the Statens Serum Institut in Copenhagen, and the Ministry of Public Health and Social Security in Madrid giving lectures and taking part in discussions and in field investigations. An epidemiologist from Instituto Superiore di Sanità was seconded to CDSC for six months.

Training and teaching The training and teaching activities of PHLS as a whole and CDSC have assumed greater importance because of the decline in available expertise in the epidemiology and control of communicable disease in the NHS. PHLS now has four full-time senior registrars in community medicine associated with CDSC, two funded by PHLS and two by NHS Regions. A scheme of short-term attachments for senior registrars in general community medicine, which began in 1978, has proved successful in providing a minimal basic training in the field investigation of incidents of communicable disease. Six senior registrars were attached to CDSC during the year.

Fourteen courses, either full or half day, were provided at the Centre mainly for groups of community physicians in training but also for visiting microbiologists, veterinary officers and environmental health officers. CDSC staff contributed to postgraduate teaching programmes at the London School of Hygiene and Tropical Medicine and the Department of Community Medicine of the Middlesex Hospital Medical School and to undergraduate teaching programmes at four London medical schools.

Communicable Disease 1980/81

THE first joint PHLS/Office of Population Censuses and Surveys annual review of communicable disease was published in 1980 for the year 1979 and a review of 1980 is in preparation; a brief summary of the main events of 1980 follows:

Brucellosis. The annual numbers of reports of human cases continued to fall; in England and Wales only 17 cases of infection with *Brucella abortus* or brucella species unspecified were reported in 1980 compared with 33 in 1979, a decrease which correlated with the brucellosis eradication scheme in cattle.

Enterovirus infections. Echovirus type 30 was the most frequently reported enterovirus infection during 1980; there were 754 reports, over half of them from patients with aseptic meningitis. The outbreak began at the end of June and continued until September and affected also Scotland and continental Europe. There were 2 cases of paralytic poliomyelitis reports in 1980.

Food poisoning. Statutory notifications, laboratory reports, and a new outbreak reporting system from medical officers for environmental health (MOsEH) were presented together weekly in the Communicable Disease Report. There was an overall decline in laboratory reports of food poisoning and in notifications but a slight increase in laboratory reports of *Salmonella typhimurium* infections; *S. hadar*, the second most

common serotype, declined. In over 20 per cent of the outbreaks reported by MOsEH a bacterial cause was not identified and some of these were probably viral gastro-enteritis; indeed in two outbreaks electron microscopy demonstrated small round particles in the faeces of cases.

In 1980 there was a large outbreak of waterborne gastro-enteritis of unknown aetiology affecting over 1000 households in Leeds associated with a sewage overflow near a bore hole water source; the episode led to a review of bore hole water sources elsewhere in the country and to reaffirmation of the responsibility of the MOEH supported by PHLS for the safety of water supplies.

Twenty-six incidents of toxic food poisoning due to scombroid fish were reported affecting over 75 people and 13 incidents of red bean poisoning affecting 47 people.

Viral hepatitis. The rise in notifications of infective jaundice which began in 1979 continued throughout 1980 and was attributed to an increase in incidence of hepatitis A. Further outbreaks of foodborne heptatitis A were reported, the most notable of which were three outbreaks in London associated with the consumption of frozen raspberries.

Influenza. Although there was little influenza in 1980/81, the winter was again unusual because two subtypes of influenza A virus circulated. In November and December outbreaks mainly amongst young people due to H_1N_1 subtype were reported; in January, however, this subtype almost disappeared and was replaced by variants of H_3N_2 subtype causing a few outbreaks in old peoples homes and schools.

Legionnaires' disease. There were 202 cases of legionnaires' disease reported in 1980, all but 7 of them due to *Legionella pneumophila* serogroup 1. There was a seasonal peak in September and October. More cases were in males than females, 2.4:1. The mean age in males was 50 years and in females 57 years. In 80 (40 per cent) cases the infection was probably acquired abroad; 25 of these were associated with an hotel outbreak in Benidorm, Spain. PHLS staff assisted the Spanish health authorities in the investigation of this outbreak which indicated that the source of infection was probably piped water in the hotel; control measures were instituted and no further cases were reported. Another notable outbreak took place in Kingston, Surrey where the infection was associated with the local district hospital; more information about this outbreak is given on page 48.

Malaria. For the first time for over a decade there was a fall in the annual number of notifications, from 1625 in 1979 to 1296 in 1980. Data from the Malaria Reference Laboratory, which included also cases which were not formally notified, showed a fall from 2054 in 1979 to 1670 in 1980. As in previous years *Plasmodium vivax* infections were the most common and accounted for 1131 of 1597 cases in which the infecting species was known. The country where the infection was probably acquired was recorded in 852 of these 1131 *P. vivax* infections; 740 (87 per cent) were from the Indian subcontinent. Of the 405 *P. falciparum* infections, the probable country of origin was recorded in 366; only 9 (2 per cent) were from the Indian subcontinent and 312 (85 per cent) from West or East Africa. These 312 cases included 7 of the 9 deaths attributed to malaria during the year.

Ornithosis. Laboratory reports of *Chlamydia B* infection in 1980 were more than double those of 1979—372 compared with 176. Although this increase may have been partly spurious due to increasing interest in laboratory diagnosis of atypical pneumonia and better laboratory reporting, it nevertheless probably represented a real increase. There were two small outbreaks of human infection associated with duck processing plants in eastern England but infection in poultry was not shown to be associated with cases elsewhere and did not explain the increase.

Sexually transmitted diseases. For the first time attendances at STD clinics in the United Kingdom exceeded half a million in 1980, a more than 5-fold increase since the 1950s. Non-specific genital infection continued to rise; there were 125 383 cases seen at clinics in 1980; an 11 per cent increase on 1979. Early infectious syphilis increased slightly to 1684 cases. Gonorrhoea declined to 60 824 cases but there was an increase in laboratory reports of β-lactamase producing strains of *Neisseria gonorrhoeae;* these rose from 104 in 1979 to 211 in 1980. Of these 211 cases, 71 (34 per cent) probably acquired the infection in the United Kingdom, most of them in the London and Liverpool areas.

Tuberculosis. Notifications of tuberculosis continue to decline slowly in England and Wales; there were 6673 notifications of respiratory tuberculosis and 2472 of non-respiratory tuberculosis in 1980 compared with 6808 and 2460 respectively in 1979. However, chest clinic returns from 1973 to 1979 do not show a decline in the number of new infectious cases (sputum smear-positive) which remains at about 2000 per year; the figure for 1980 is not yet available. In January 1981 CDSC established laboratory reporting of *Mycobacterium tuberculosis* which it is hoped will provide more information about this core of infectious cases and lead to the final control of the disease in England and Wales.

REGIONAL AND AREA LABORATORIES

THE number of specimens received by regional and area laboratories during 1980 was, at just over 6 million, about 4 per cent greater than the number recorded for 1979 (Figure 2). Table 3 shows the numbers for various categories of specimen; the numbers are derived from analysis of a 1 per cent sample of each laboratory's records so that in some cases they may be distorted when the numbers are small. Most categories shared in the small increase with the somewhat surprising exception of rubella serology, with about 713 000 specimens compared with about 783 000 in 1979. Other analyses show that about 73 per cent of the sera sent for rubella antibody determinations to determine the need for immunization came from pregnant and about 20 per cent from non-pregnant women. No fewer than 1.7 m specimens of urine were received, an increase of about 9 per cent over 1979.

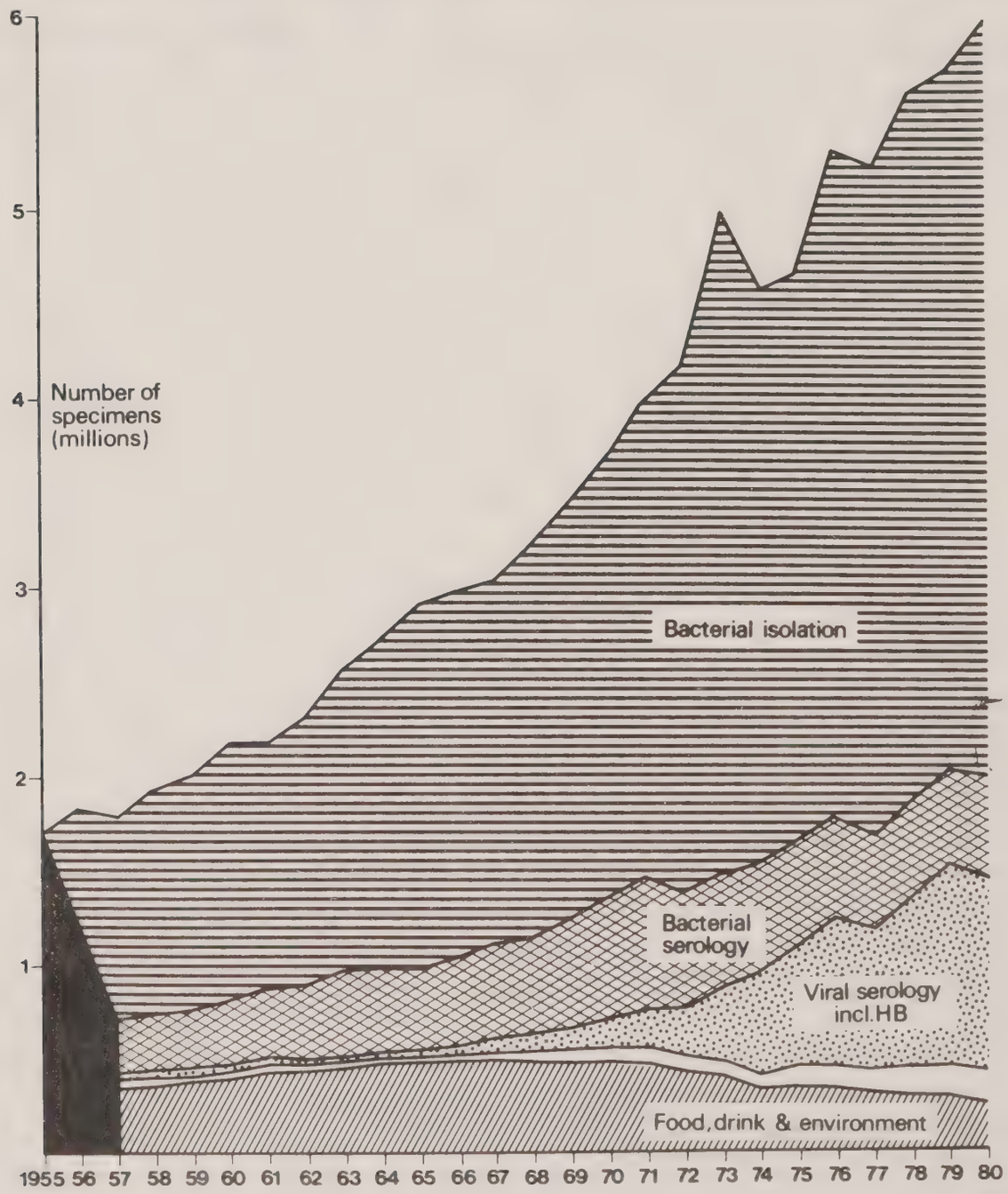

Figure 2: Numbers of different types of specimens examined in PHLS Regional and Area laboratories.

Table 3 Specimens examined in Regional and Area Laboratories, 1980

Source	*Examination*	*No. of specimens*	*Totals*
Humans	Isolation of bacteria		
	Nose, throat and mouth	255 654	
	Sputum (excluding tb)	157 257	
	Faeces, rectal swabs	348 806	
	Urine	1 721 321	
	Blood cultures	164 818	
	Others	1 156 899	3 804 755
	Sputum for tuberculosis	125 767	125 767
	EM virus diagnosis	28 726	28 726
	Isolation of virus/chlamydia	136 616	136 616
	Detection of antibody/antigen		
	Venereal diseases	392 738	
	Other bacterial	77 922	
	Rubella	713 174	
	Hepatitis	139 912	
	Other virus	175 381	
	Toxoplasma	19 308	1 518 435
	Antibiotic assays	18 582	18 582
Animals		1 535	1 535
Food	Milk	53 790	
	Ice-cream	14 389	
	Other food	54 034	
	Drinking water	71 077	193 290
Other sanitary	Bathing water	30 007	
	Other	63 697	93 704
Total			*5 921 410*
Reference specimens, various			82 540
Grand total			*6 003 950*

In all, 32 of the 52 laboratories recorded an increased number of specimens; in two cases substantial increases resulted from local reorganization of laboratory services. In at least one laboratory a useful reduction in workload has been achieved by a concerted effort to ensure that unsatisfactory specimens were rejected and to educate the clinical staff in the most effective use of the laboratory services.

Some of the more specialised activities of individual laboratories are illustrated in Table 4. The great majority are now undertaking virus isolation and no fewer than 33 have access to an electron microscope for attempted demonstration of viral infection. The diagnostic services for virus infections are generally available to other laboratories in the neighbourhood and several (e.g. Bristol and Leeds) provide such services for very wide areas. The other principal reference services provided by public health laboratories to other laboratories in PHLS and in the hospital service are listed in Table 3.

Table 4 also indicates some of the principal research topics being pursued in the laboratories. The list of topics, abridged for purposes of presentation, is selective and incomplete. Most laboratories are involved in clinical trials or laboratory testing of new antibiotics on some scale and these projects are not included in the list. Similarly many laboratories are investigating new or improved methods for isolation or recognition of microbes, or for determination of antibody levels; many of these studies are carried out in collaboration by a number of laboratories.

Table 4 Regional and Area Laboratories: special facilities and research topics

Laboratory	*No. of specimens 1980*	*Diagnostic facilities for virology*			*Reference services for other laboratories*	*Principal current research topics*
		Electron microscopy	*Culture*	*HBsAg*		
Bath	101 647	+	+	+	–	Campylobacter epidemiology; amoebae in hot springs; hygiene of hydrotherapy pools; human milk banks
Birmingham	253 942	+	+	+	Mycobacteria	Antibiotic sensitivity testing and assays; legionella; hepatitis A & rotavirus infections (in associated RHA Regional Virus Lab)
Brighton	108 483	+	+	+	–	Gastroenteritis in children
Bristol	176 842	+	+	+	Chlamydia; syphilis serology; gonococcal plasmid typing	Treponemal immunobiology; gonococcal and chlamydial infections; viral gastroenteritis
Cambridge	172 348	+	+	+	Legionella; streptococcus gp A; hepatitis	Impedance and conductivity studies of blood cultures; quality of antimicrobial discs; leukaemia antigen; lymphomas in transplant patients
Carlisle	65 072	–	–	+	Fungal serology	Dermatophyte infections
Chelmsford	94 029	+	+	+	–	–
Chester	120 418	+	+	–	–	Listeria in pregnancy; anaerobes in urine
Coventry	122 882	+	+	–	Klebsiella typing	Laboratory autoclaves; group B and group F streptoccal infections
Dorchester	57 822	+	+	+	–	Salmonellas in meat
Epsom	74 940	+	+	+	Coxsackie A viruses	Viruses & diabetes; campylobacter infections
Exeter	105 150	+	+	+	–	Work-load measurement; influenza; isolation of treponemes; streptococcal infections in military camps

Gloucester	82 060	–	+	–	–	–
Guildford	70 023	+	+	+	*Shigella sonnei;* fungal chemotherapy	Influenza
Hereford	46 990	+	+	–	–	Campylobacter infections; salmonellas in poultry
Hull	26 015	–	–	–	–	Salmonellas in the food chain and environment; non-bacterial gastro-enteritis
Ipswich	121 745	–	–	+	–	Surveys of human milk banks and of goats' milk supplies
Leeds	173 399	+	+	+	Food microbiology; toxoplasma; viruses (includes Category A lab); tubercle bacilli; streptococcus gp A; anthrax	Cytomegalovirus in pregnancy; legion-ellae in amoebae; pneumococcal vac-cine; toxoplasma antigens and diag-nosis; salmonellas and *E. coli* in foods
Leicester	87 571	+	+	+	Yersinia	Pilot computer day-book; hepatitis B in pregnant women and subnormal children
Lincoln	67 135	–	–	–	–	Travellers' diarrhoea
Liverpool	143 898	+	+	+	Mycobacteria; VD serology	Chlamydial infections; salmonellas in hospital; legionella infections; diag-nosis of gonorrhoea
London: C. Middlesex	96 365	+	+	+	–	Mycobacteria in water; viral gastro-enteritis; streptococcal endocarditis; automation and minicomputers
London: Dulwich	58 888	+	+	+	Mycobacteria	Human milk banks; *M. tuberculosis* in different ethnic groups
London: Tooting	68 346	–	–	+	Toxoplasma	Toxoplasma antigen and epidemiology; use of microcomputer; gp A strepto-cocci in general practice; staphylococci in endocarditis; yersinia in faeces
London: Whipps Cross	86 487	–	+	+	–	Human milk bank; *Clostridium difficile*
Luton	70 994	–	+	+	Anaerobic bacteria	Anaerobic infections: campylobacter infections

Maidstone	70 325	–	–	+	Cholera and other vibrios	Antigens and ecology of *V. cholerae* and related vibrios
Manchester	151 613	+	+	+	Meningococci; mycobacteria; campylobacter typing; food microbiology	Campylobacter infections; meningococcal antigens and epidemiology; immunofluorescence and RIA for viral antibodies; hepatitis associated with blood products
Middlesbrough	118 957	+	+	+	–	Hygiene in catering; biliary tract infection
Newcastle	176 551	+	+	+	Syphilis serology; mycobacteria sensitivity testing; staphylococcal phage typing; chlamydia isolation	Bacteriuria in schoolgirls; experimental virus infections of CNS; anaerobic infections and activity of polymorphonuclear leukocytes
Norwich	147 709	–	+	+	(Mycoplasma Reference Lab)	Low temperature/steam and formaldehyde disinfection; ornithosis associated with ducks; computer for routine laboratory use
Nottingham	267 126	+	+	+	Legionella	Isolation and characterization of legionellas; automation for urine bacteriology
Oxford	265 320	+	+	+	Streptococci gp A; Legionella	Automation and rapid methods for bacteriology; streptococcal infections; experimental virus infections of CNS
Peterborough	80 335	–	+	+	–	–
Plymouth	145 467	–	–	+	–	Anaerobes in tonsils
Poole	148 952	–	+	+	–	Automation for bacteriuria; food hygiene norms; microbiology of cosmetics
Portsmouth	153 541	+	+	+	Brucella	Serology of bacteroides; gas liquid chromatographic analysis of vibrios and bacteroides; microbiology of continuous ambulant peritoneal dialysis fluids

Preston	128 700	+	+	+	Brucella; legionella	Rotavirus infections; serology of legionellosis; CMV infections; campylobacter growth requirements
Reading	126 873	+	+	+	–	Group B streptococci in neonates; viruses in sewage
Salisbury	43 269	+	+	+	–	Food hygiene; campylobacters in milk
Sheffield	216 199	+	+	+	Haemophilus species	Influenza; pneumococcal vaccines; ultra-clean air in operating rooms; urinary infections in patients with spinal injury
Shrewsbury	98 103	+	+	–	–	Influenza; laboratory autoclaves
Southampton	194 516	–	+	–	–	Campylobacters; lysozyme in tear-fluid
Stoke on Trent	136 806	–	+	+	–	GLC in clinical microbiology; *M. kansasii* in water
Taunton	74 194	–	+	+	Farmers' lung serology	Throat infections in schoolchildren; chlamydial infections
Truro	104 913	–	–	+	–	Campylobacter infections
Watford	57 243	–	–	+	–	–
Wolverhampton	85 671	–	–	+	–	Isolation of chlamydia; studies of ELISA techniques
Cardiff	148 356	+	+	+	(Mycobacterium Reference Unit) Streptococci gp A	Isolation of salmonellas; influenza; serological tests for rickettsias; opportunist mycobacteria and sensitivity testing of *M. tuberculosis*
Carmarthen	35 505	+	+	+	–	Zoonoses in general practice; chlamydial respiratory infections
Conwy/Rhyl	41 443	+	+	–	–	Water in home dialysis units and hospitals
Swansea	46 407	+	+	+	Toxoplasma; diphtheria bacilli	ELISA for toxoplasma, rubella and CMV; toxoplasma antigens

THE NATIONAL SURVEY OF INFECTION IN HOSPITALS, 1980

Dr P D Meers, Division of Hospital Infection

THE control of infection is taken into account in the design of much hospital activity. Despite this, there is a surprising ignorance of the true extent and character of infection in hospitals. Without information about its frequency and the diseases that contribute to it, any attempts at control seem likely to be ill-founded. To gather the necessary basic information, a small multi-disciplinary group planned a survey of hospital infection. The group, which included NHS representation, was set up by the PHLS, and the survey was carried out between May and July, 1980.

The survey was designed as a prevalence or cross-sectional study. It covered 18 163 patients occupying acute beds in 43 district general and teaching hospitals. The hospitals, geographically spread to coincide with the main centres of population, were selected according to certain criteria, including a willingness to participate and the existence in them of a Control of Infection Officer and an Infection Control Nurse. These persons, together with a member of the nursing staff of each ward as it was involved, constituted the survey team for each hospital.

Each team visited an average of just over 400 patients. The distribution by speciality of the beds surveyed was arranged so that the final sample was nationally representative. The teams recorded data relevant to all the patients visited, in a standard way. In each case a judgement was made, according to fixed criteria, on whether the patient was suffering from an infection, and if so, of which system and with which microbe. Any antimicrobial treatment being given was noted. The infections that were diagnosed were separated according to their probable acquisition in the community (community acquired infection, CAI) or in hospital (HAI). The information necessary to each decision was extracted from medical and nursing records, temperature charts, and laboratory and X-ray reports, and where necessary, the patient was examined.

Consistency among the 43 teams was facilitated by using standard protocols and record sheets, and by training at least one member of each team in the techniques to be used. In addition, 11 specially trained, medically qualified observers were appointed in the various regions. These individuals supervised the beginning of each survey in from two to five hospitals, to reinforce the other measures.

The recording system allowed for the ready extraction by hand of any information required by individual hospitals, from the data they had collected. However, the large number of records made during the whole survey were analysed with the help of PHLS Computer Services.

The results showed that, at the time, 19.1 per cent of the patients surveyed were judged to have an infection. Of these 9.9 per cent were thought to have been brought into hospital from the community, and the remaining 9.2 per cent to have been acquired in hospital. The prevalence of all infections in the different hospitals varied between 3.6 per cent and 28.6 per cent, with CAI varying between 1.2 per cent and 17.5 per cent and HAI between 2.4 per cent and 16.9 per cent.

Respiratory infection was overall the most prevalent, much of it classified as CAI. Among the HAI cases, the most prevalent was urinary tract infection (in 2.8 per cent of patients), followed by respiratory tract infection (upper in 0.3 per cent of patients, lower in 1.5 per cent), wound infection (1.7 per cent), infection of the skin and subcutaneous tissues (1.2 per cent) and finally a miscellaneous group of individually infrequent infections (1.6 per cent). This distribution is illustrated in Figure 3.

It is hoped that the information derived from the survey will be used to justify the allocation of resources to hospital infection control, to help in locating areas where this is

waste, and to guide decisions on priorities. It is also seen as a baseline for further studies of the components of, and means to be used for, preventing hospital infection, and for the education of all concerned. The latter is the area in which the greatest impact is foreseen. Nearly all the infections recorded were of the unremarked, endemic variety, and were not associated with identified outbreaks. Endemic infection of this kind tends to be taken for granted by hospital doctors and nurses, who as a result may deny the existence of HAI which they recognise only in epidemic form. Education leading to a wider recognition of the scale of endemic HAI is likely to encourage the acceptance of measures designed to control it.

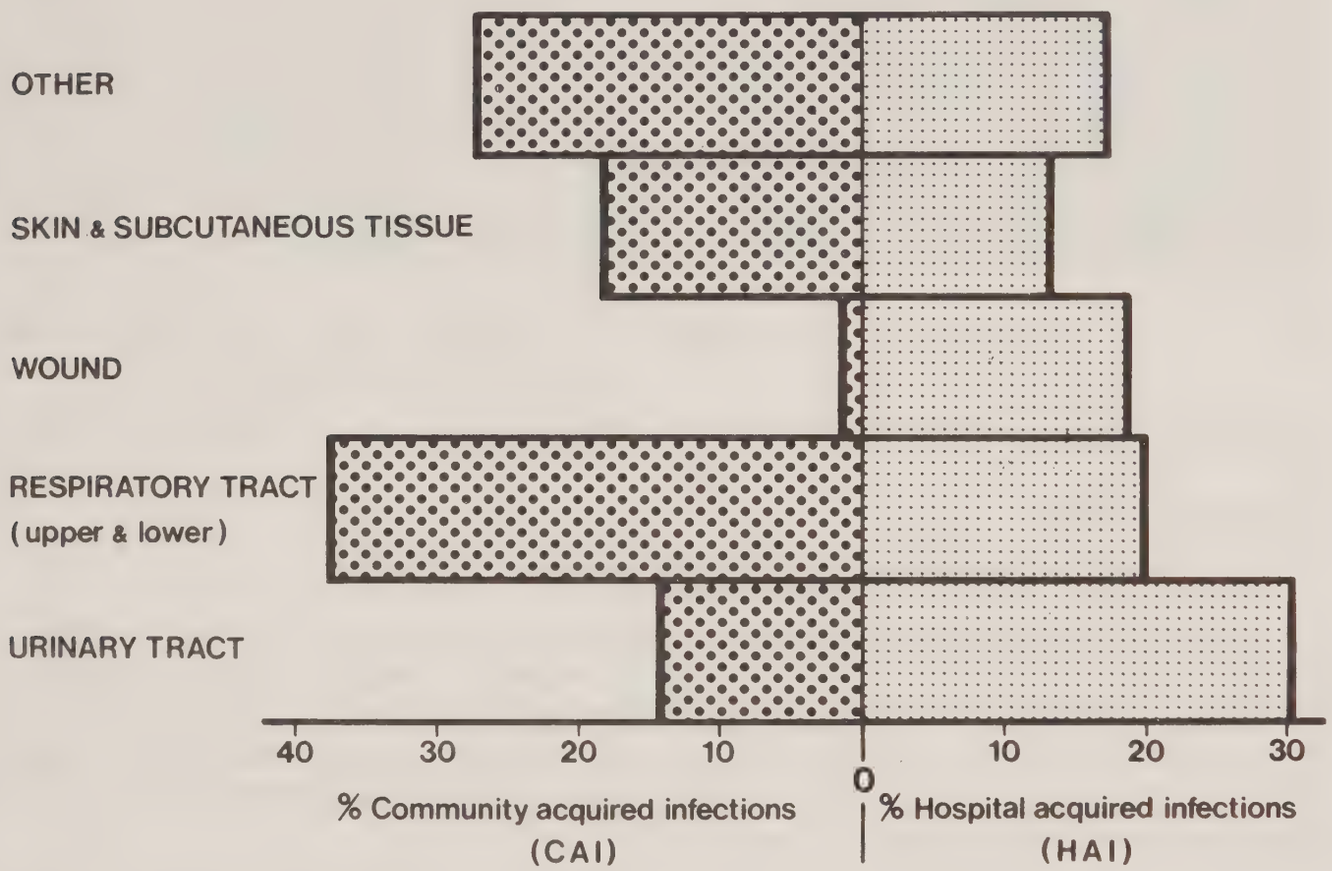

Figure 3: Prevalence of various infections among 18 163 acute hospital patients in 43 hospitals in England and Wales, 1980.

VIRUSES IN FOODBORNE GASTROENTERITIS

Dr Hazel Appleton, Virus Reference Laboratory, Colindale

IN 1980 a new reporting system for foodborne outbreaks of gastroenteritis was set up by the PHLS Communicable Disease Surveillance Centre. Although foodborne outbreaks are commonly assumed to be bacterial in origin, in almost a quarter of outbreaks reported in 1980 bacterial pathogens were not isolated and interest has recently focused on the possible involvement of viruses. Viruses have already been implicated in two large community outbreaks associated with cockles in England in 1976 and oysters in Australia in 1978.

The viral agents which have recently been associated with foodborne gastroenteritis have not been cultured in the laboratory, and are usually detected by electron microscopy where they appear as small round particles. Since it was demonstrated that viruses were most probably responsible for the large cockle-associated outbreak of 1976, the Virus Reference Laboratory in collaboration with colleagues in various other PHLS Laboratories has examined specimens from several further outbreaks where no bacterial food poisoning organisms could be detected. The electron microscopy results are summarised in Table 5.

Table 5 Viruses in foodborne gastroenteritis (1977 – 1980)

Food implicated	*Number of outbreaks*	*Number of patients tested (faeces)*	*Number excreting small round viruses*
Shellfish: Cockles	8	86	75 (87%)
Oysters	2	8	7 (88%)
Various (not shellfish)	5	53	12 (23%)

These outbreaks were all characterised by a very high attack rate and incubation period of 24 hours or more, longer than that normally associated with bacterial food poisoning. Symptoms included both vomiting and diarrhoea. Virus particles were observed in faecal specimens from a large proportion of people who were ill after eating shellfish, but viruses have not so far been firmly linked with gastroenteritis occurring after the consumption of other types of food.

Unlike bacteria, viruses do not multiply in foods and, if present, are likely to be few. Electron microscopy is a relatively insensitive technique and so it is difficult to detect virus in food samples. Bivalve molluscs however, are able to concentrate micro-organisms from surrounding water, and virus particles similar to those observed in faecal specimens from patients were detected in oysters in one recent outbreak.

The shellfish incriminated in all the outbreaks were bacteriologically satisfactory, but it would appear that procedures for the depuration of oysters or heat treatment of cockles were indadequate for the removal of viruses. Unfortunately until it becomes possible to culture these agents, testing suspected food samples remains unrewarding.

Viruses that have been implicated in foodborne outbreaks are not those normally associated with infantile gastroenteritis such as rotavirus, adenovirus or astrovirus. In outbreaks described here small, round, featureless viruses were observed (Figure 4.1). These resemble parvoviruses and are morphologically similar to viruses previously seen in several outbreaks of winter vomiting disease. Small, round, structured viruses (Figure 4.2) similar to the Norwalk agent have been observed in outbreaks of nonbacterial gastroenteritis in Britain, but not so far in outbreaks where foodborne transmission was

suspected. However, such viruses have been incriminated in an outbreak associated with oysters in Australia and in waterborne outbreaks in the United States.

Seventy-five outbreaks of unknown aetiology were reported to CDSC in 1980, and of those for which information was available, more than one third had a long incubation period suggestive of viral gastroenteritis.

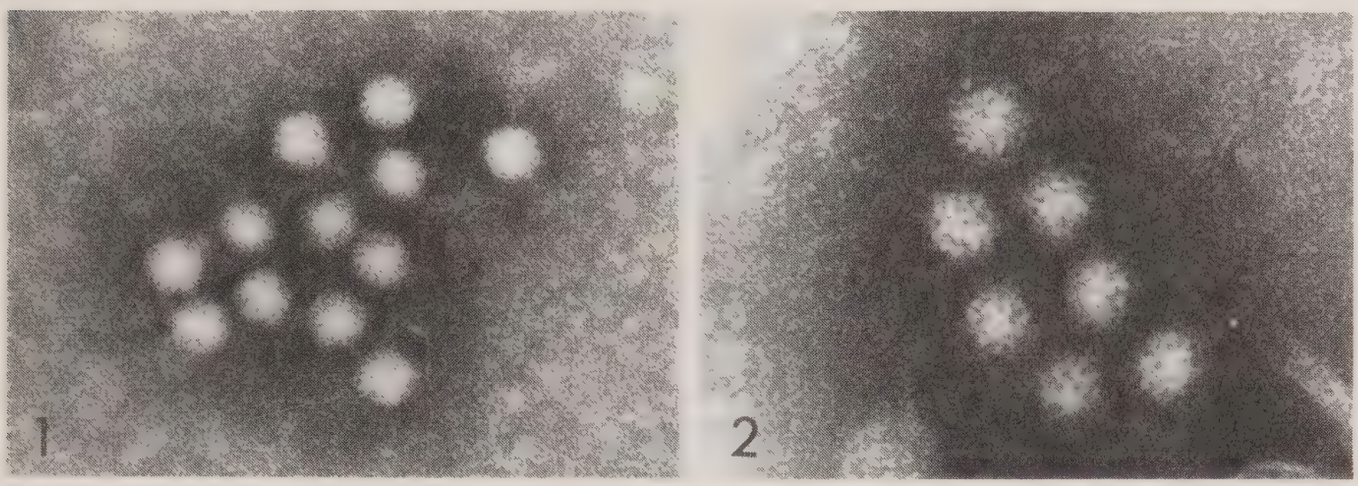

Figure 4: Viruses in foodborne gastroenteritis

1. Small round featureless viruses from an outbreak of gastroenteritis associated with eating cockles. Magnification ×189 000.
2. Small structured viruses from an outbreak of non-bacterial gastroenteritis. Magnification ×189 000.

LEGIONNAIRES' DISEASE IN ENGLAND AND WALES 1980

Epidemiological aspects

Dr C L R Bartlett, PHLS Communicable Disease Surveillance Centre, Colindale

TWO hundred and two cases of legionnaires' disease were reported in 1980. Serogroup 1 infections predominated; only seven were reported due to other serogroups. The diagnosis was established usually by serology but in seven cases *L. pneumophila* was isolated from lung (biopsy 1, post-mortem 6) and in two others the bacterium was demonstrated in lungs by immunofluorescence staining. One hundred and sixteen patients showed four-fold or greater rises in antibody titres by immunofluorescence to at least 1 in 64; 56 had convalescent titres of at least 1 in 128 and 44 had titres of 1 in 256 or more. The remaining 21 cases showed rising titres to less than 1 in 64 in paired sera, or had convalescent titres of less than 1 in 128 and so did not meet fully the criteria for diagnosis of the infection.

All 202 patients had pneumonia, most with segmental or lobar consolidation. In 128 cases more detailed information about the clinical features is available from the PHLS collaborative study of legionnaires' disease. Seventy five patients (59 per cent) became confused and 11 showed other signs of central nervous system involvement including ataxia, dysarthria and paraesthesia. Gastrointestinal symptoms were common, 50 patients (39 per cent) having vomiting and 42 (33 per cent) diarrhoea. A rash, usually described as maculo-papular, was reported in 25 (20 per cent); eight developed renal failure.

The number of cases reported to CDSC has increased steadily from 25 in 1977, to 77 in 1978 and to 127 in 1979. This trend probably reflects the greater interest of clinicians and availability of diagnostic reagents rather than a real change in the incidence of the disease. Male cases exceeded female cases by a ratio of 2.4:1; the mean age for males was 50 years and for females 57 years.

The infection was probably acquired abroad in 80 cases, 25 of which were associated with an outbreak in a hotel in Benidorm, Spain. Other countries associated with clusters among British tourists included Portugal, Greece and the United States of America. As in earlier years, there was a distinct seasonal pattern with few cases in the early months of the year and peak incidence in the late summer and autumn.

Several small clusters of nosocomial infection were reported and an outbreak of 11 cases occurred in one district general hospital. Altogether 24 patients were thought to have acquired their legionella infection in hospital, mostly while in-patients under investigation or treatment for other conditions. Eight of the cases in the district general hospital were patients but one was a visitor and two were members of staff. Epidemiological and environmental studies implicated the hospital plumbing system as the principle source of the infection; chlorination of the cold water supply and raising the hot water temperature seemed to be effective in terminating the outbreak.

There were 25 deaths in the 202 cases during 1980, including ten in those who acquired the infection in hospital, but it is not clear how many were directly attributable to the legionella infection. Of the 20 fatal cases among the 128 cases in the PHLS collaborative study, 15 had other pre-existing diseases; in nine of these it was chronic respiratory disease. Only 38 of the 108 survivors are known to have underlying disease.

Laboratory Aspects

Dr A G Taylor, Division of Microbiological Reagents and Quality Control, Colindale

Serological diagnosis The difficulty in culturing *Legionella* from clinical specimens has ensured the continuing importance of the serological diagnosis of legionnaires' disease (LD). Most cases (> 90 per cent) in England and Wales are still diagnosed by the indirect fluorescent antibody test using formolised yolk sac antigen (FYSA) prepared by the Division of Microbiological Reagents & Quality Control (DMRQC). FYSA, in use since January 1978, has continued to prove specific and sensitive, and most PHLS and some other laboratories now offer this test as a routine investigation. Problems of differentiating LD from other respiratory tract infections have been shown to be minimal when FYSA is used; it does not show the serological cross-reactions found in other tests for LD.

Because antibody titres as high as 16 are uncommon in control subjects, a presumptive diagnosis of LD may be made early in the disease as low titres may nevertheless indicate infection. Use of the antigen may also reveal occasional cases caused by strains of *L. pneumophila* other than serogroup 1, although these are better revealed by specific serogroup antigens. Serogroup 2–6 antigens have been made available to PHLS laboratories at Cambridge, Oxford, Nottingham and Preston, which provide reference facilities for LD. Of 1792 sera submitted in 1980 to DMRQC for LD serology, only 2 were ascribable to infection by serogroups other than serogroup 1, suggesting that routine testing of sera for non-serogroup 1 infections in all diagnostic laboratories would be uneconomic.

A polyvalent *L. pneumophila* (serogroups 1–6) antiserum is available for detection of the organism in clinical and environmental samples and for confirmation of the identity of isolates.

Antigens to *Legionella* species other than *L. pneumophila* are being evaluated in DMRQC.

Culture and collection of strains The culture medium recommended by Greaves (PHLS Nottingham) has been used with success in several laboratories. This and other recently described media have facilitated the direct culture of *L. pneumophila* from clinical specimens.

The Bacterial Metabolism Research Laboratory has continued to confirm the identity of strains by gas-liquid chromtography and the National Collection of Type Cultures has strains submitted from clinical and environmental sources, preserved for future study.

Research and development Research has continued on the development of a rapid diagnostic method based on the detection of specific antigen in tissues.

Methods for isolation of legionellas from environmental sources have been refined at PHLS Oxford, allowing further investigations of the occurrence of legionellas in water storage and distribution systems. The association of *L. pneumophila* with various amoebae has been reported from PHLS Leeds; other studies on this are planned in various laboratories.

PENICILLINASE-PRODUCING GONOCOCCI IN BRITAIN

Dr A E Jephcott, PHLS, Bristol

WHEN penicillin was first used for treatment for gonorrhoea all strains seemed highly sensitive, but after 10 years use gonococci showing some lessening in susceptibility were observed. From then on the numbers of these strains and their resistance have increased.

This change has resulted from a series of chromosomal mutations making the bacterial cell less susceptible to the drug. It has proceeded at different rates throughout the world, and relatively few organisms encountered in Britain, are, at present, sufficiently indifferent to penicillin to render ineffective the traditional 'one shot' therapy, when the largest possible doses are given. It must be stressed that even these organisms are still susceptible to pencillin provided an adequate concentration can be reached at the site of the infection and that penicillin is the treatment of first choice for gonorrhoea in Britain.

In 1976 an entirely new development was recognised. Strains of gonococci that were totally resistant to penicillin because of production of a penicillin destroying enzyme (pencillinase) appeared. This resistance is determined by extra-chromosomally sited plasmids which can be passed to other bacteria and spread resistance rapidly by this means. It soon became apparent that two different types exist. One appears to have originated from West Africa and carries a 3.2 megadaltons (Mu) plasmid. A focus of these strains was detected in Liverpool. At almost the same time, other strains were recognised after being imported into North America. These originated in the Far East and carry a 4.4 Mu plasmid determining resistance. This is frequently accompanied by a 24.5 Mu transfer factor, which together with a much lower spontaneous rate of loss of resistance than is shown by the African type, had led them to be regarded with even more concern. Soon chains of infection were detected where no foreign source could be identified. In the United Kingdom, by contrast, for the first two years strains could be traced to importations of the less worrying African types.

Table 6 Penicillinase-producing gonococci in UK 1977 – 1980: presumed source of infection

	No of reported infections				*Total*
	1977	*1978*	*1979*	*1980*	
Abroad*	8	21	68	131	228
United Kingdom	5	8	21	50	84
Not known	2	2	15	30	49

* This total includes cases infected in UK by consorts infected abroad (1,3,13,21 = 38)

Table 7 Penicillinase-producing *Neisseria gonorrhoeae* 1977 – 1980: area of origin of cases presumed infected abroad

Area of infection	*No of reported cases*				*Total*
	1977	*1978*	*1979*	*1980*	
Africa	5	9	17	37	68
Far East	2	7	31	49	89
Other and not stated	0	2	7	24	33

The predominance of the African plasmid in the UK has not lasted. Figures compiled by the PHLS Communicable Disease Surveillance Centre and the PHLS Venereal Diseases Reference Laboratory reveal a steady increase in the proportion of strains originating from the Far East. The absolute number of penicillinase producing organisms detected has risen from 15 in 1977 to 211 in 1980, at which time 36 per cent of imported strains had been traced to West Africa and 47 per cent to the Far East (See Tables 6 and 7).

These observations have now been extended by the Bristol PHLS Laboratory working in conjunction with the Microbiology Department of Bristol University. Examination of the plasmid types of strains isolated throughout the country shows that both Asian and African plasmid types are present in approximately equal numbers (see Table 8). Further, a small focus of endogenous infection with the Asian plasmid has occured in one of our cities.

In Holland one further complication has been recognised. Strains of gonococci have been discovered which carry not only the African resistance factor but also the Asian transferring ability. These are viewed with concern because it must be inferred that genetic transfer between the original strains has occurred and that transfer to other gonococci must be a real possibility. These strains have not been discovered in Britain to date.

The present situation must cause concern, but rapid detection of penicillinase producing strains is readily available from most PHLS and many AHA laboratories. This should allow effective treatment and control in this country, and monitoring of the plasmid carriage will be continued in our effort to understand the natural history of the development of resistance in the bacterial kingdom.

Table 8 Distribution of plasmids in a sample of penicillinase-producing *Neisseria gonorrhoeae* isolated in UK 1977 – 1981

Source	*Plasmid size Mu*			
	No	*3.2*	*4.4*	*24.5(+)*
Africa	6	6	–	–
Far East	14	–	14	9
United Kingdom	15	7	8	5
Other	3	1	2	1

(+) Transfer factor, found only in association with 4.4 Mu plasmid.

PHLS INTERNATIONAL WORKSHOP ON CAMPYLOBACTERS

Dr A D Pearson, PHLS Southampton

THE meeting, which was held over three days at the University of Reading, took the form of ten workshop sessions, and was limited to investigators actively engaged in work with the these bacteria. Sessions were devoted to the following topics: global epidemiology; serology and serotyping; taxonomy, typing and growth requirements; pathogenicity in humans and animals; clinical aspects; molecular biology; public health measures; and epidemiology and environmental aspects. The papers, demonstrations and discussions at the workshop demonstrated the world-wide interest in campylobacter infections. The extent and limitations of present knowledge are made clear in the questions and answers that summarised the final session under the title: 'Campylobacters—where do we go from here?' These were:

Where do they come from? Although there are well-documented common source outbreaks associated with the consumption of contaminated water, milk and poultry and some evidence for case-to-case spread and for human infections from domestic pets, most cases of campylobacter infection are 'sporadic'. A better understanding of the routes of infection depends on the development of serological typing and of enrichment techniques. This should enable a more adequate investigation of cases, their contacts and suspected source materials.

How do they cause disease? It is clear that not everyone who is infected with *Campylobacter jejuni* develops symptoms and not all cases present with diarrhoea. Further work is needed to establish the dose-related attack rates, the extent of immunity resulting from previous infection and the role of the organism in other pathological conditions. Markers for pathogenicity should be investigated since not all strains of *C. jejuni* may be pathogenic for humans.

What should we be saying to clinicians? *C. jejuni* enterocolitis is usually an unpleasant but self-limiting disease. In the majority of cases no specific treatment will be indicated since, by the time a bacteriological diagnosis is available, the diarrhoea will have responded to symptomatic treatment or remitted spontaneously. The proper role of erythromycin in the treatment of *C. jejuni* infection is a matter for debate. It may be useful in selected cases where symptoms are severe or prolonged or to limit the duration of excretion. Some erythromycin-resistant strains have been isolated and, although at present such strains are uncommon, irresponsible use of erythromycin may prejudice the value of this antibiotic in the future.

What should we be saying to Health Authorities? In many countries *C. jejuni* is a major cause of infective enteritis in humans, probably accounting for as many cases as other intestinal bacterial pathogens, in particular salmonellas and shigellas. There is a need to support research to develop an internationally recognised serotyping scheme so that full epidemiological investigations can be carried out. The importance of the large number of strains which can be isolated from farm animals and poultry and from environmental sources should be assessed. Research is also needed into better laboratory techniques for the isolation of the organism and for the detection of antibodies as a measure of past or current infection.

The procedings of the workshop will be published in January 1982 by MTP Press Ltd, Lancaster, under the title of—*Campylobacter: epidemiology, pathogenesis and biochemistry,* price £29.95.

HONOURS, AWARDS, AND EXTERNAL OFFICES

Sir Robert Williams	Chairman, Genetic Manipulation Advisory Group; President, Association of Clinical Pathologists; First Ledingham Lecturer, University of Aberdeen.
Dr C L R Bartlett	Honorary Lecturer, Department of Environmental & Preventive Medicine, Medical College of St. Bartholomew's Hospital, University of London; Temporary Adviser, Regional Office for Europe, World Health Organization.
Dr J R H Berrie	Member, Advisory Group on the Antigenic Composition of Influenza Vaccine, DHSS.
Mr R Brooks	Vice-Chairman, Medical Laboratory Technicians Board, Council for Professions Supplementary to Medicine.
Dr K A Cammack	Visiting Lecturer, Smith College Clark Science Center, Northampton, Mass. USA.
Dr R Y Cartwright	Chairman, Microbiologists Group, South West Thames Region.
Dr E O Caul	Member, Interim Advisory Committee on Class II Microbiological Safety Cabinets, DHSS; WHO Fellowship at Caribbean Epidemiology Centre, Trinidad.
Mr B S Chessum	Member, Regional Council, Institute of Medical Laboratory Sciences.
Dr C Dulake	Member, Standing Advisory Committee on Laboratory Staffing and Organization, Royal College of Pathologists.
Dr J M B Edwards	Member, Committee on Development of Vaccines and Immunization Procedures: Epstein-Barr Virus, Medical Research Council.
Professor D C Ellwood	Honorary Professor, University of Warwick; Visiting Professor, Karolinska Institute, Stockholm; Member of Court, University of Bath; Member Genetic Manipulation Advisory Group; Member, Editorial Board, *Biotechnology Letters*; Member, Working Party on Social Dimensions of Biotechnology, Commission of the European Communities.
Mr C G T Evans	Member, Scale-up Subcommittee, Genetic Manipulation Advisory Group.
Dr A E Flower	Clinical Teacher, University of Leicester Medical School.
Dr N S Galbraith	Member, Council of the British Society for the Study of Infection; President, Infection Control Nurses Association; Member of Council, Society of Community Medicine; Honorary Senior Lecturer in Community Medicine, London School of Hygiene and Tropical Medicine; President, Section of Epidemiology & Community Medicine, Royal Society of Medicine.
Dr P S Gardner	Member, Working Party on Quality Assurance and Member of Council, European Committee on Clinical Laboratory Standards; Chairman, Scientific Group on Rapid Laboratory Techniques for the Diagnosis of Viral Infections, World Health Organization.
Dr S D Gardner	Member, Advisory Group on Rabies; Member, Advisory Group on Slow Viruses; Member, *Papovaviridae* Study Group, Vertebrate Virus Subcommittee, International Committee on the Taxonomy of Viruses; Member, Safety Committee, London Licensed Teachers of Anatomy; Member, Joint British Medical Association/British Veterinary Association Zoonoses Committee.

Dr G L Gibson	Member, Executive Committee of Council, Royal College of Pathologists; President-Elect, East Mercian Branch, Association of Clinical Pathologists.
Dr R J Gilbert	Fellow, Pharmaceutical Society.
Dr J V T Gostling	Chairman, Laboratory Services Subcommittee, East Anglican Regional Health Authority.
Dr J B Griffiths	Deputy Chairman, European Society for Animal Cell Technology; Secretary European Federation of Cell and Virus Collections.
Dr P Hambleton	Lecturer in Biochemistry, Salisbury College of Technology.
Mr G J Harper	Temporary Adviser, Special Programme on Safety Measures in Microbiology, World Health Organization.
Dr R J C Hart	Honorary Research Fellow, University of Exeter.
Dr L R Hill	Member, United Kingdom Committee, Commonwealth Collections of Microorganisms.
Mr B Holmes	Member, ad hoc Commissions of the International Committee for Systematic Bacteriology (Subcommittee on the Taxonomy of Enterobacteriaceae) on: *Klebsiella—Enterobacter—Hafnia-Serratia;* and on *Proteus—Providencia.*
Dr W L Hooper	Member, Committee F (Pharmacy) British Pharmacopoeia Commission
Dr C H L Howells	Member, Manpower Advisory Panel, Royal College of Pathologists; Fellow, Institute of Biology.
Dr P A Jenkins	Member, Editorial Board, *Journal of Medical Microbiology.*
Miss Deborah Lewis	J D Atkinson Award 1980.
Dr M J Lewis	Editor, *Journal of Hygiene.*
Mr P D Littlejohns	Chairman, Birmingham Branch, Institute of Medical Laboratory Sciences.
Professor J Melling	Honorary Visiting Professor and Nelson Distinguished Lecturer in Biology, Rutgers University, USA; Secretary, Biotechnology Group, Society of Chemical Industry; Member, Committee on Development of Vaccines and Immunisation Procedures, DHSS/MRC.
Dr N D Noah	Honorary Senior Lecturer in Clinical Epidemiology, Royal Free Hospital.
Dr W K Paver	Member, National Advisory Committee (Virology), Institute of Medical Laboratory Sciences.
Dr J H Pennington	Chairman, North West Epidemiology Club.
Dr M S Pereira	Member, Trials Subcommittee, MRC Committee on Influenza and Other Respiratory Virus Vaccines; Member, Advisory Group on Influenza Vaccination, DHSS; Co-director, Collaborating Centre for Reference and Research on Influenza, World Health Organization.
Dr C Philpot	Member, Standing Advisory Committee of Associates, Royal College of Pathologists.

Mr J A Pinegar	Lecturer (part-time), Department of Life Sciences, Leeds Polytechnic.
Dr C D Ribeiro	Clinical Teacher, Welsh National School of Medicine.
Dr C Roberts	Adviser in Postgraduate Education for Mersey Region, Royal College of Pathologists.
Dr A Robinson	Member, Committee, Cell Surfaces and Membrane Group, Society for General Microbiology.
Dr B Rowe	Chairman, Global Scientific Working Group and Member, Steering Committee, Diarrhoeal Diseases Programme, World Health Organization; Visiting Consultant, Pan American Health Organization.
Dr J B Selkon	Chairman, Research Committee and Member of Council, British Thoracic Association.
Dr D I H Simpson	Visiting Professor, London School of Hygiene and Tropical Medicine, University of London; Fellow, Institute of Biology.
Dr P M Sutton	Member, Board of Governors, Salisbury College of Technology.
Dr D R Telford	Clinical Lecturer, University of Leeds.
Mr R Van Hegan	Lecturer, Sheffield Polytechnic.
Dr E M Vandervelde	Member, Advisory Group on Testing for Hepatitis B, DHSS.
Dr H E Wade	Member, Advisory Committee of the National Pituitary Collection; Member, Human Growth Hormone Committee, DHSS.
Dr J G Wallace	Medical Advisor, Anglian Water Authority.
Dr J E M Whitehead	Member of Council, Royal College of Pathologists.
Dr A T Willis	Medical Administrator, Luton & Dunstable Hospital.
Dr Geraldine Willshaw	Member, Editorial Board, *Journal of General Microbiology.*
Dr A E Wright	Temporary Adviser, Special Programme on Safety Measures in Microbiology and Informal Consultation on Mammalian Safety of Microbiological Agents for Vector Control, World Health Organization.
Dr S E J Young	Honorary Consultant Physician, Coppetts Wood Hospital.

STAFF CHANGES

New Appointments

Dr E J Threlfall	Principal Microbiologist, Division of Enteric Pathogens, Central Public Health Laboratory, Colindale. 1.4.80.
Mr P Murphy	Deputy Secretary to the Board. 1.4.80
Ms C Richmond	Publications Editor, PHLS Board. 1.5.80.
Mr P P Taylor	Personnel Officer, PHLS Board. 13.8.80.
Dr W A Telfer Brunton	Consultant Medical Microbiologist, Director, Area Public Health Laboratory, Truro. 1.10.80.
Professor A A Glynn	Consultant Medical Microbiologist, Director, Central Public Health Laboratory, Colindale. 1.10.80.
Dr D G E Newell	Principal Microbiologist, Area Public Health Laboratory, Southampton. 13.10.80.
Dr D R Telford	Consultant Medical Microbiologist, Regional Public Health Laboratory, Leeds. 1.11.80.
Dr K A V Cartwright	Consultant Medical Microbiologist, Director, Area Public Health Laboratory, Gloucester. 1.1.81.
Dr S I Egglestone	Principal Microbiologist, Regional Public Health Laboratory, Bristol. 1.1.81.
Dr A P C H Roome	Consultant Virologist, Regional Public Health Laboratory, Bristol. 1.2.81.

Transfers

Dr P G Higgins	Consultant Virologist; secondment (on leave of absence) to WHO, Trinidad. 31.7.80.
Dr E R Mitchell	Consultant Medical Microbiologist, Area Public Health Laboratory, Maidstone. 2.11.80. For duties at the William Harvey Hospital, Ashford.
Dr D A Robinson	Consultant Epidemiologist; secondment to WHO, Geneva. 4.1.81.

Resignations

Dr J O'H Tobin	Director, Public Health Laboratory, Oxford. 31.8.80.
Dr K Sargeant	Director, Microbial Products Development & Production Laboratory, CAMR. 21.1.81.
Dr B R Eaton	Director, Public Health Laboratory, Watford. 31.3.81.
Dr J A Rycroft	Consultant Medical Microbiologist, Public Health Laboratory, Chelmsford. 31.3.81.

GRANTS AND OTHER ASSISTANCE RECEIVED OR RENEWED FOR SPECIAL INVESTIGATIONS

The Public Health Laboratory Service Board received valuable assistance from the following bodies for the assistance of special investigations and the acquisition of major equipment of a special nature:

From the World Health Organization:

$3000 for Influenza Surveillance and Research by the WHO Collaborating Centre for Reference and Research on Influenza, at the Virus Reference Laboratory, Central Public Health Laboratory, under the joint direction of Dr M S Pereira and Dr J J Skehel.

$2000 for the preparation and testing of reagents by the Division of Microbiological Reagents and Quality Control, under the direction of Dr P S Gardner.

$3750 for the WHO Collaborating Centre for Reference and Research on Hospital Infection, at the Division of Hospital Infection, Central Public Health Laboratory, under the direction of Dr P D Meers.

$6500 for the WHO Collaborating Centre for Phage-Typing and Resistance of Enterobacteria at the Division of Enteric Pathogens, Central Public Health Laboratory, under the direction of Dr B Rowe.

From Laboratoire de Recherche API:

£6640 for the study of the value of API strips in the identification of anaerobes, by the Bacterial Metabolism Research Laboratory, under the direction of Dr M J Hill.

From Wessex Regional Health Authority:

Up to £6000 from 1.12.80 to 30.9.81 for research on the use of microbial enzymes as diagnostic reagents for the determination of drug levels in blood, by Mr P M Hammond at the Diagnostic Reagents Laboratory, CAMR, under the direction of Dr A Atkinson.

From the Cancer Research Campaign:

£79 758 from 1.10.80 to 30.9.81 for research on bacteria and the etiology of cancer at the Bacterial Metabolism Research Laboratory under the direction of Sir Robert Williams and Dr M J Hill.

From the Medical Research Council:

Dr J Craske, Regional Public Health Laboratory, Manchester: £21 133 for 2½ years from 1.3.80 for a study on acute hepatitis in a defined population in general practice in North West England.

Dr A Atkinson, Director, Diagnostic Reagents Laboratory, CAMR: £56 703 over 3 years for research on triazine dye adsorbent chromatography, and the purification of therapeutic and diagnostic proteins.

Dr P D Marsh, Pathogenic Microbes Research Laboratory, CAMR: £28 144 over 3 years for research on the effect of different environmental conditions on the phenotypic expression of oral streptococci.

From the Lister Institute of Preventative Medicine:

Dr G Murray, Division of Microbiological Reagents and Quality Control, Central Public Health Laboratory, for the research into the rapid serological diagnosis of rubella (by studying the kinetics of the interaction of rubella virus specific antigen and early antibody).

From the Department of Health and Social Security:

Dr P D Meers, Director of the Division of Hospital Infection, Central Public Health Laboratory, Colindale: £11 800 for financial year 1980/81, in support of a prevalence survey of hospital acquired infection in England and Wales.

CDSC under the direction of Dr N S Galbraith: £24 819 over 3 years for a study of clinical illness in boarding school children.

A clause in Schedule 3 of the National Health Service Act 1977 permits the Board to accept, hold and administer private gifts on trust for any purpose related to the Public Health Laboratory Service or otherwise connected with microbiological research. Donations received during the year ending 31 March 1981 were as follows:

£4728 from the British Diabetic Association for research at the Area Public Health Laboratory, Epsom.

£4000 from La Roche & Co Ltd for research at the Bacterial Metabolism Research Laboratory, Colindale.

£4320 from Glaxo Limited for research at BMRL, Colindale.

£1068 from the University of London for research at the Bacterial Metabolism Research Laboratory, Colindale.

£2160 from the European Economic Commission for research at the Centre for Applied Microbiology and Research, Porton Down.

£50 from the Association of Clinical Pathologists for the PHLS General Endowment Fund.

£1000 from the Oxford Streptococci Conference for the PHLS General Endowment Fund.

£720 from the London Zoo for the Marmoset Fund of the Central Public Health Laboratory, Colindale.

£489 from the Nuffield Nursing Home for research at the Area Public Health Laboratory, Newcastle.

£850 from the Roussel Laboratories for research at the Area Public Health Laboratory, Nottingham.

£80 from Dr M J Lewis for the staff fund at the Area Public Health Laboratory, Nottingham.

£20 from the British Broadcasting Corporation; £20 from Imperial Chemical Industries Ltd., for the Central Library, Colindale.

£310 from Hampshire Area Health Authority for research at the Area Public Health Laboratory, Portsmouth.

£5 from Dr D Payne for research at the Area Public Health Laboratory, Portsmouth.

£20 from Glaxo Ltd.; £15 from Dr Pereira; £36 from the University of Khartoum for rabies research at the Central Public Health Laboratory, Colindale.

PUBLIC HEALTH LABORATORY SERVICE BOARD PUBLICATIONS

These publications can be purchased from the Government Bookshops in London (post orders to PO Box 569, SE1 9NH). Edinburgh, Cardiff, Belfast, Manchester, Birmingham and Bristol, or through booksellers. *Prices do not include postage*

Catalogue of the National Collection of Type Cultures 1972		£2.50

Monograph Series

No. 1	Laboratory Diagnosis of Venereal Disease	50p
No. 2	The Use of Chemical Disinfectants in Hospitals	50p
No. 3	Anaerobic Bacteria	*Second edition due Spring 1982*
No. 4	The Distribution and Identification of Non-Fermenting Bacteria	80p
No. 5	Laboratory Methods 1 (Elek's test for the toxigenicity of corynebacteria; The isolation and identification of *Listeria monocytogenes;* The culture and identification of mycobacteria; infectious mononucleosis; Isolation of lactobacilli from the genital tract)	50p
No. 6	The Prevention of Laboratory Acquired Infection	£1.50
No. 7	Preservation of Bacteria, with notes on other micro-organisms	£1.50
No. 8	Isolation of Salmonellas	£1.50
No. 9	The Trichomonads	£2.00
No. 10	The Bacteriological Examination of Urine: report of a workshop on needs and methods	£2.00
No. 11	The Vibrios	£2.00
No. 12	Basic Serodiagnostic Methods for Diseases Caused by Fungi and Actinomycetes	£2.50
No. 13	The Laboratory Diagnosis of Toxoplasmosis	£2.00
No. 14	Benchbook on Brucella	£3.00
No. 15	Isolation and Identification of Ringworm fungi	£3.50
No. 16	Laboratory Investigation of Rubella	*due late 1981*
No. 17	Haemophilus influenzae	*due late 1981*
No. 18	Immunofluorescence Techniques in Microbiology	*due Spring 1982*

PUBLICATIONS BY MEMBERS OF THE STAFF OF THE PUBLIC HEALTH LABORATORY SERVICE DURING 1980

In addition to the items mentioned below, there are many publications to which the work of the Service has contributed. The internationally recognised reference laboratories and the Communicable Disease Surveillance Centre submit figures regularly to WHO for inclusion in their statistical periodicals. Again, the giving of specialist help and advice and the supply of serological reagents are among the functions of the Service, and in the course of the year a number of papers have acknowledged such contributory work by members of the staff. Other unlisted material includes leading articles, unsigned annotations, conference papers which remain unpublished, book reviews, contributions to the various abstracting journals, and notes in the Service's weekly Communicable Disease Report.

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